integritybio

Final Report

Compatibility Examination for CHS-1701
Version 2

October 2, 2015

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1. Executive Summary

The stability of CHS-1701 when stored in representative container closure systems (both borosilicate glass and media bag) over a 30 hour period was assessed. This was performed with reversed-phase HPLC (RP-HPLC), size-exclusion HPLC (SE-HPLC) analyses, and High Accuracy liquid particle count (HIAC), which have been shown to be effective stability-indicating assays for the product.

During the course of the study, all samples remained clear, without discoloration, and free of visible particulates. API concentrations remained consistent during the 30 hour study, within Coherus' specification of 10.0 ± 1.0 mg/mL.

Physical stability, as determined by SE-HPLC, indicated no significant physical changes to CHS-1701 as a result of container closure system, or due to the duration of incubation within these containers. Main peak percentages of samples from both container closure systems were within Coherus' specification of ≥ 95.0%.

Chemical stability, as determined by RP-HPLC, showed no significant changes to CHS-1701 as a result of either container closure system, or due to duration of incubation within these containers. Main peak percentages were within Coherus' specification of ≥ 90.0%.

HIAC results, regardless of incubation time or container closure system, resulted in values below the USP <788> specifications for both 10 µm and 25 µm bin sizes.

Based on the results of this study, CHS-1701 BDS in its current formulation remained within Coherus' specifications during storage in either a sterile glass vial or a pre-sterilized HyClone BPC Media Bag for up to 30 hours at ambient temperature.

2. Study Design

2.1 Study Objective

To assess the stability of Pegfilgrastim when stored in representative vessels (both glass and bag) over a 30 hour period. The following were the specific aims to be achieved in this study:

- To determine the effects of storage at ambient temperature within a BPC Media Bag or Borosilicate glass vial.
- To detect key degradation products of CHS-1701.

2.2 Experimental Design

2.2.1 Materials

The active pharmaceutical ingredient (API) presented in this report is CHS-1701,a Pegfilgrastim (PEGylated recombinant human granulocyte colony-stimulating factor (GCSF). The details of the CHS-1701 bulk drug substance (BDS) and Reference Standard (RS) material utilized in the study are listed below:

CHS-1701 BDS:	10 mg/mL CHS-1701 in 10 mM sodium acetate, 5% Sorbitol, 0.004% (w/v) Polysorbate 20 (P20), pH 4.0. Batch #169A14-02, Item #25002.
CHS-1701 RS:	10 mg/mL CHS-1701 in 10 mM sodium acetate, 5% Sorbitol, 0.004% (w/v) Polysorbate 20 (P20), pH 4.0. Lot #BET-09 April 2015.

The CHS-1701 BDS and RS were provided by Coherus. The BDS material was stored at 2-8°C until use. The RS material was stored at -70°C, and allowed to thaw at 2-8°C until use.

The materials used to prepare the CHS-1701 samples analyzed in this study were as follows:

(1) Filter	CellSmart, 250-mL, 0.2 µm PVDF, Catalog #BPV2225, Lot #130709-054
(2) Media Glass vial	Corning, Catalog #1395-100, Lot #04115001
(3) Media Bag	Pre-sterilized HyClone BPC, 100-mL, Part #SH3B6501, Lot #EZK196227, Expiration: October 2017
(4) Stoppers:	Daikyo 13 mm injection stopper, Fluorotec Plus®, B2-40
(5) Syringes	Heinke Sass Wolf, 30-mL Norm-Ject, Catalog #CE0535, Lot #13B158B
	Heinke Sass Wolf, 10-mL Norm-Ject, Catalog #CE0123, Lot #5F13048
(6) Syringe Needles	Becton-Dickenson 18G x 1 ½", Catalog #BD305196, Lot #5059501
(7) Vials:	Schott borosilicae 10-cc, 13mm serum (West Pharmaceutical)

2.2.2 Formulation Parameters

In this study, the following formulation parameters were fixed for CHS-1701:

(1) API Concentration:	10 mg/mL CHS-1701
(2) Buffer:	10 mM Sodium Acetate
(3) Tonicity Modifier:	5% (w/v) Sorbitol
(4) Surfactant:	0.004% (w/v) Polysorbate 20
(5) pH:	4.0
(6) Fill Volume:	90 mL

2.2.3 Sample Preparation

200-mL of Coherus' BDS was allowed to equilibrate to room temperature prior to vacuum filtration at 75 torr via a 0.2 µm PVDF filter.

Working within a Class II Type BSC, a total of 90-mL of filtered product was transferred into a 100-mL media bag via one of the two self-sealing feed lines using a non-silicone coated 30-mL syringe and an 18G x 1 ½" needle. The feed line was then clamped off during the duration of the study. The second feed line served as the port for sample extractions at each time point in this study. This second line was clamped off in between each time point. Although the feed lines were self-sealing, clamps were used to avoid leakage.

While continuing to work within a Class II Type BSC, a total of 90-mL of filtered product was transferred into a sterilized 100-mL glass vial using a non-silicone coated 30-mL syringe and an 18G x 1 ½" needle.

Both the media bag and glass vial remained in the Class II Type BSC at ambient temperature (~23°C) throughout the duration of the 30 hour study.

At each time point, ~7 mL of drug product was sampled from both the media bag and glass vial using a non-silicone coated 10-cc syringe and an 18G x 1 ½" needle, and expelled into sterile 10-cc depyrogenated borosilicate vials and stoppered within the BSC. From this sample, approximately 800 µL was transferred to a sterile 1.65-mL Eppendorf tube for all non-HIAC analyses. The remaining volume was dedicated for HIAC analyses.

Prior to HIAC analysis, samples were degassed at 75 torr for thirty (30) minutes to remove air bubbles.

Due to time required for sampling and sample preparations for the various assays, HIAC and SE-HPLC analyses of samples were performed 30-60 minutes after sampling. RP-HPLC analysis was performed on samples stored at 2-8°C for one week following sampling.

2.2.4 Stress Studies

CHS-1701 DP (10 mg/mL Pegfilgrastim, 10 mM sodium acetate, 5% (w/v) sorbitol, 0.004% polysorbate 20, pH 4.0), stored in a glass vial or media bag, was exposed to ambient temperature storage conditions under fluorescent light within the BSC over the course of 30 hours. At varying time points during storage, aliquots were aseptically sampled from each container as outlined in Table 1.

Table 1: Conditions for the CHS-1701 Compatibility Evaluation

Storage Container	Time Points
Glass Vial	0, 6, 12, 24 and 30 Hours
Media Bag	

2.2.5 Analytical Methods

The analytical methods used in this study are summarized in Table 2.

Table 2: Analytical methods for CHS-1701 analysis

Analytical Method	Purpose
Visual inspection	Clarity and color
Spectrophotometry (protein concentration by A280)	Concentration analysis
SE-HPLC per Document #AM.AL.0028.00	Oligomer and cleavage analysis
RP-HPLC per Document #AM.AL.0033.00	Degradation product analysis
HIAC, (5 ml method, via 1 ml sips)	Subvisible particle counting

The following assays were used to analyze the individual formulations:

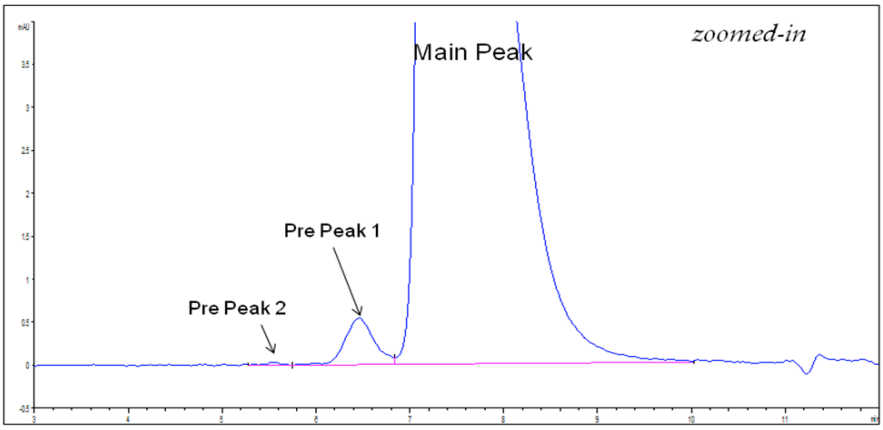
(1) Visual Inspection: Visual inspections were performed under a white light source (a 13 W fluorescent tube) against a white and black background by two different analysts. Digital photographs were acquired.

(2) Absorbance Spectrophotometry: CHS-1701 concentration was determined by measuring sample absorbencies at 280 nm and 320 nm, for protein concentrations with adjustment for light obscuration, respectively, using a Beckman spectrophotometer, where an extinction coefficient of 0.86 $(mg/mL)^{-1}$ cm^{-1} was used for concentration calculations.

(3) SE-HPLC:

- Mobile Phase: 5:95 Ethanol:100mM Sodium Phosphate pH 6.5
- Column: SEPAX SRT SEC-300, 7.8 x 30 cm, 5 µm, 300 Å
- Instrument: Agilent 1100 HPLC system
- Mode: Isocratic
- Flow rate: 1.0 mL/minute
- Total run time: 20 minutes
- Column Temperature: 25°C
- Autosampler Temperature: 5°C
- Detection: 280 nm (4 nm bandwidth)
- Sample load: 50 µg (analyzed undiluted)

Figure 1: SE-HPLC chromatogram illustrating the integration for CHS-1701



(4) RP-HPLC:

- Mobile phase A: 0.1% TFA in MQ water
- Mobile phase B: 0.1% TFA in 100% acetonitrile
- Column: RESTEK Viva C18, 250 x 4.6 cm, 5 µm, 300Å (Catalog #9514575)
- Instrument: Agilent 1100 HPLC

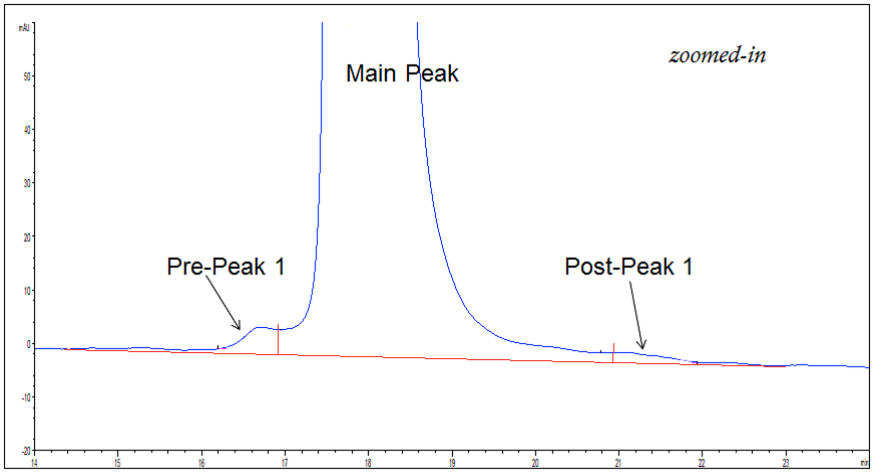
- Column temperature: 60ºC
- Autosampler Temp: 4°C
- Flow rate: 0.6 mL/min
- Time: 40 minutes
- Absorbance Detection: 215 nm

Gradient:

Time (min)	% A	% B
0	45.6	54.4
2	45.6	54.4
20	36.6	63.4
30	27	73
32	45.6	54.4
40	45.6	54.4

- Sample load: 50 µg per injection (diluted from 10 mg/mL to 0.6 mg/mL with Coherus diluents)
- Coherus Diluent: 10 mM Acetic Acid, 5 % (w/v) sorbitol

Figure 2: RP-HPLC chromatogram illustrating the integrations for CHS-1701



(5) HIAC, low volume method: Counts of subvisible particles through measurement of light obscuration were collected using a HIAC 9703 Particle Counting System. A total of 10.0 mL oof sample was analyzed by HIAC. Five runs were measured at 1.0 mL volume per run and 5.0 mL was consumed by the instrument. First and final runs were omitted from analysis due to potential artifacts generated during sample introduction and sample depletion.

2.2.6 Assay Acceptance Criteria

Acceptance criteria for each of the assays, provided by Coherus, is listed in Table 3.

Table 3. Acceptance Criteria for CHS-1701 Methods

Assay	Specification	Method Variability
A280/Protein Concentration	10.0 ± 1.0 mg/mL	± 3%
SE-HPLC	Main Peak ≥ 95.0%	Main Peak RSD <0.2%
RP-HPLC	Main Peak ≥ 90.0%	Main Peak RSD ≤ 0.2%
HIAC	≤ 6000 particles of ≥ 10 µm ≤ 600 particles of ≥ 25 µm	N/A
Visual Inspection	Essentially free of visible particulates	N/A

3. Results and Discussion

3.1 Stability Overview

This section summarizes the stability of CHS-1701 stored over 30 hours at ambient temperature in a glass vial or media bag.

3.1.1 Effect of Containers

At time zero, samples from both storage containers were clear with no visible particles. All subsequent time point samples from either storage container appeared clear and free of visible particulates with no visible changes in appearance when compared to their respective time zero samples. Photographs of the samples following storage in the media bag and glass vial are shown in Figures 3 and 4, respectively.

Figure 3. Visual analysis of CHS-1701 extracted from media bag

Specifications: Essentially free of visible particulates

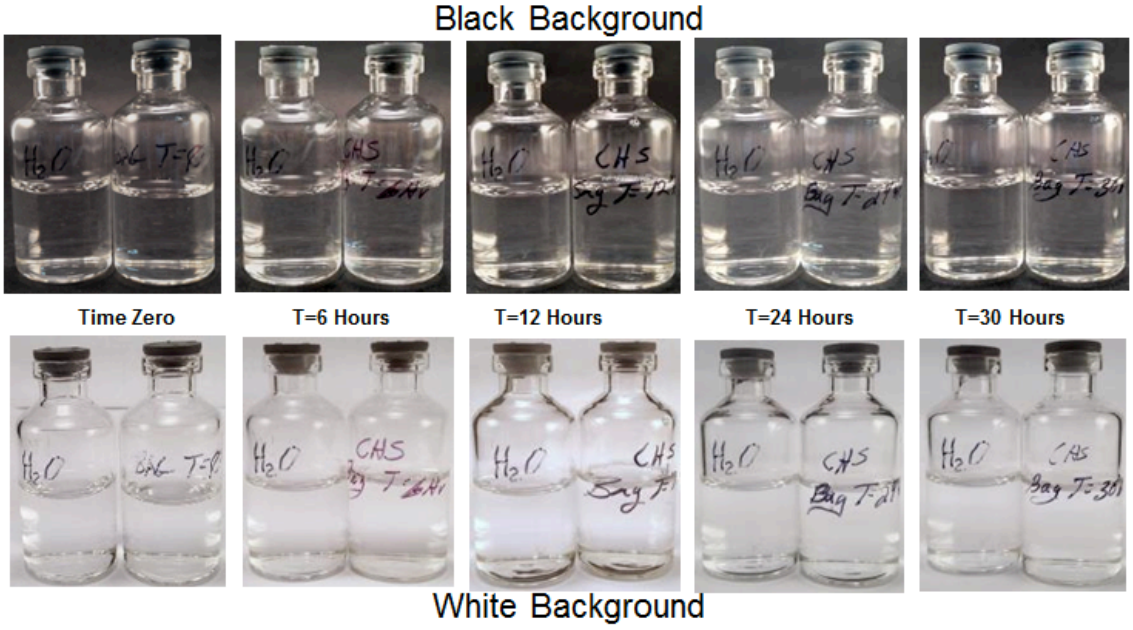
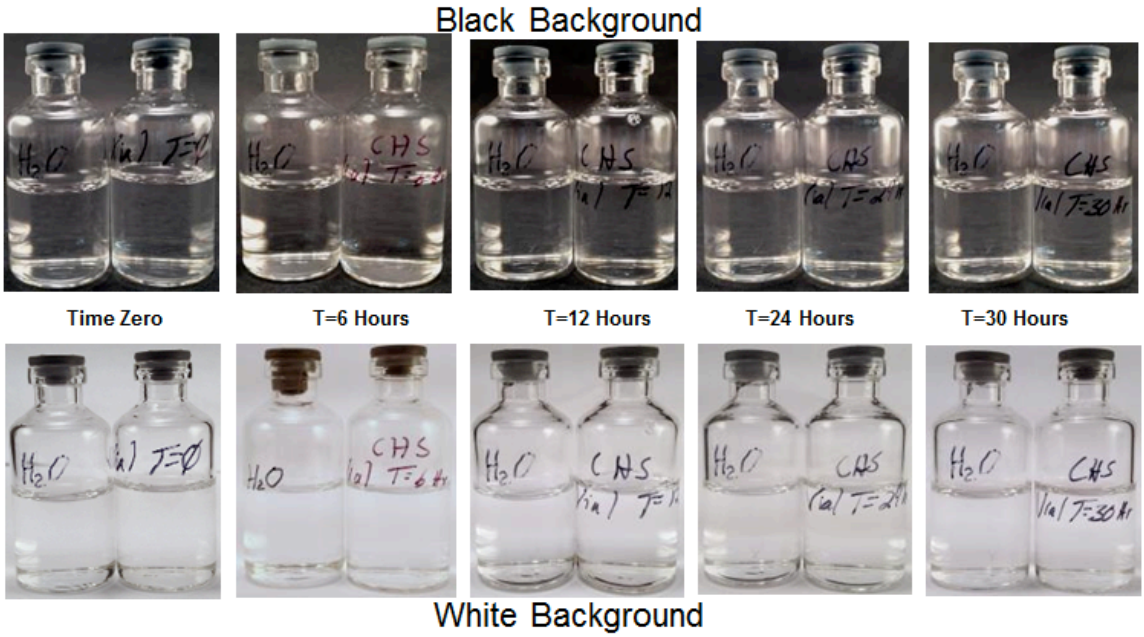


Figure 4. Visual analysis of CHS-1701 extracted from glass vial

Specifications: Essentially free of visible particulates



At each time point, samples were analyzed for absorbance at both 280 nm and 320 nm to determine the protein concentration with adjustment for light obscuration. Samples were diluted 10-fold gravimetrically using a buffer diluent (10 mM Acetate, 5% Sorbitol, 0.004% PS20, pH 4.0). The concentration measurements of CHS-1701 from both storage containers are outlined in Table 4.

Table 4. Concentration of CHS-1701 at various time points per storage container

Specifications: 10.0 ± 1.0 mg/mL; Method Variability: ±3%

Sample	Replicate 1			Replicate 2			Average
	A_{280}	A_{320}	Conc. x DF (mg/mL)	A_{280}	A_{320}	Conc. x DF (mg/mL)	Conc. (mg/mL)
Media Bag – Time Zero	0.4204	0.0024	9.9	0.4236	0.0048	9.9	9.9
Media Bag – T=6 Hrs	0.4377	0.0068	10.0	0.4383	0.0075	9.9	9.9
Media Bag – T=12 Hrs	0.4220	0.0013	9.8	0.4222	0.0015	9.8	9.8
Media Bag – T=24 Hrs	0.4182	0.0019	9.8	0.4187	0.0016	9.8	9.8
Media Bag – T=30 Hrs	0.4198	0.0020	9.9	0.4167	0.0016	9.8	9.9
Glass Vial – Time Zero	0.4123	0.0019	9.7	0.4124	0.0020	9.7	9.7
Glass Vial – 6 Hrs	0.4144	0.0018	9.7	0.4147	0.0018	9.7	9.7
Glass Vial – 12 Hrs	0.4166	0.0042	9.8	0.4178	0.0050	9.8	9.8
Glass Vial – 24 Hrs	0.4182	0.0023	9.8	0.4161	0.0009	9.8	9.8
Glass Vial – 30 Hrs	0.4198	0.0059	9.9	0.4183	0.0051	9.8	9.8

The concentrations values observed after 30 hours from samples extracted from either storage container were comparable to their respective concentrations of CHS-1701 at time zero. All concentration values were within the method variability (±3%) and no significant differences were observed between the two different storage containers and no significant changes were observed over 30 hours.

CHS-1701 samples were also analyzed via SE-HPLC. The resulting SE-HPLC chromatograms and tabular data of CHS-1701 samples stored for 30 hours are shown in Figure 5 and Table 5, respectively.

Figure 5. SE-HPLC chromatograms of CHS-1701 during 30 hours incubation

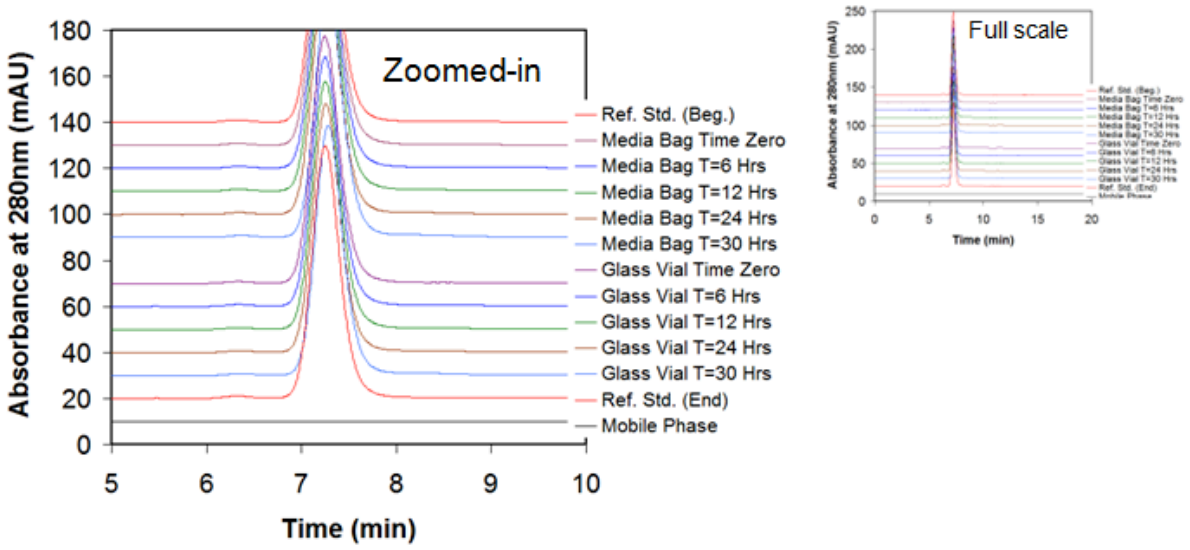


Table 5. SE-HPLC Tabular Results of CHS-1701 after 30 hours incubation

Specifications: Main Peak ≥ 95.0%; Method Variability: Main Peak RSD <0.2%

Sample	Pre-peak 2 %	Pre-peak 1 %	Main peak %	Total area (mAu)
Reference Standard (Beg.)	0.09	0.9	99.1	2388
Media Bag – Time Zero	0.02	0.7	99.3	2350
Media Bag – T=6 Hrs	0.02	0.6	99.3	2354
Media Bag – T=12 Hrs	0.04	0.7	99.3	2377
Media Bag – T=24 Hrs	0.04	0.7	99.3	2368
Media Bag – T=30 Hrs	0.05	0.7	99.2	2377
Glass Vial – Time Zero	0.02	0.7	99.3	2349
Glass Vial – 6 Hrs	0.02	0.7	99.3	2387
Glass Vial – 12 Hrs	0.04	0.7	99.3	2361
Glass Vial – 24 Hrs	0.02	0.7	99.3	2378
Glass Vial – 30 Hrs	0.03	0.7	99.2	2373
Reference Standard (End)	0.12	0.9	99.0	2402

Over 30 hours of storage, samples stored in either a media bag or glass vial at ambient temperature both resulted in percentage purities by SE-HPLC comparable to values observed at time zero results. All main peak percentages were within the method variability (Main Peak RSD < 0.2%) and no significant differences were observed between the two different storage containers and no significant changes were observed over 30 hours.

RP-HPLC analysis was employed to monitor for chemical degradation of CHS-1701. The RP-HPLC chromatograms and peak area percentages of the two containers over 30 hours of incubation at ambient temperature are shown in Figure 6 and Table 6, respectively.

Figure 6: RP-HPLC chromatograms of CHS-1701 during 30 hours incubation

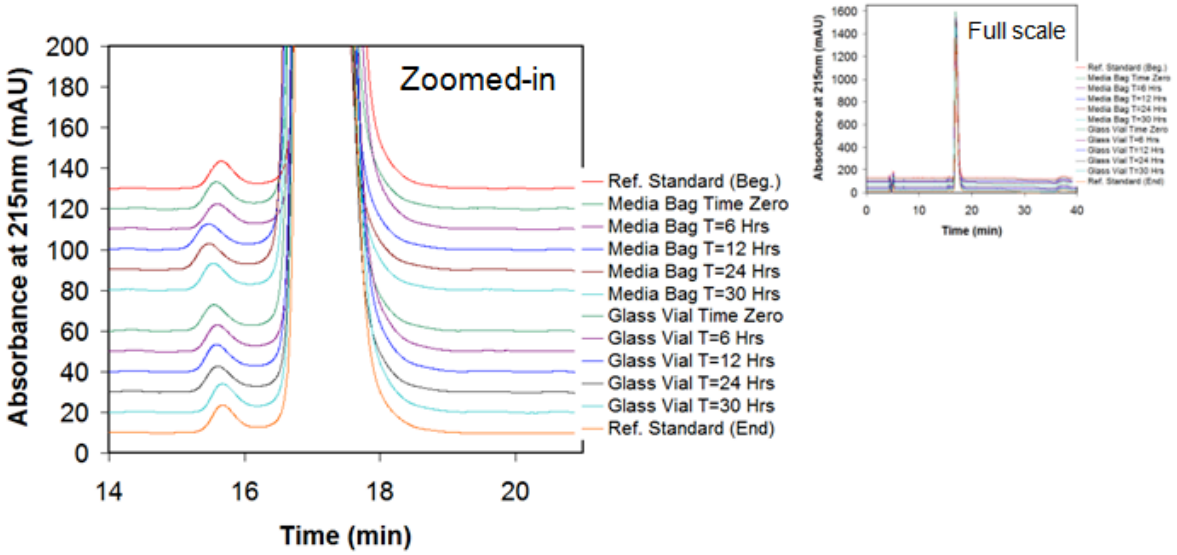


Table 6: RP-HPLC Tabular Results of CHS-1701 after 30 hours incubation

Specifications: Main Peak ≥ 90.0%; Method Variability: Main Peak RSD ≤0.2%

Sample	Pre-peak %	Main peak %	Post-peak %	Total area (mAu)
Reference Standard (Beg.)	0.8	99.0	0.1	47476
Media Bag – Time Zero	0.8	99.0	0.2	51412
Media Bag – T=6 Hrs	0.8	99.0	0.2	51220
Media Bag – T=12 Hrs	0.8	99.0	0.2	51859
Media Bag – T=24 Hrs	0.8	99.0	0.2	51436
Media Bag – T=30 Hrs	0.8	99.0	0.2	51083
Glass Vial – Time Zero	0.8	99.1	0.2	51213
Glass Vial – 6 Hrs	0.8	99.0	0.3	50770
Glass Vial – 12 Hrs	0.8	99.0	0.2	52017
Glass Vial – 24 Hrs	0.8	99.0	0.2	51051
Glass Vial – 30 Hrs	0.8	99.0	0.2	51807
Reference Standard (End)	0.8	99.0	0.1	47314

Over 30 hours of storage, samples stored in either a media bag or glass vial at ambient temperature both resulted in main peaks comparable to those observed at time zero. All main peak percentages were within the method variability (Main Peak RSD ≤0.2%) and no significant differences were observed between the two different storage containers and no significant changes were observed over 30 hours.

Low volume HIAC analysis was performed to assess subvisible particles in the samples. Tables 7 and 8 show the HIAC results over the 30 hour study in the media bag and glass vial,

respectively. All samples, regardless of incubation time or container closure system, resulted in values below the USP <788> specifications for both 10 µm and 25 µm bin sizes.

Table 7: HIAC results of CHS-1701 during 30 hours incubation in media bag

Specifications: ≤ 6000 particles of ≥ 10 µm and ≤ 600 particles of ≥ 25 µm

Time point	Sample	≥ 10 µm particles/mL			≥ 25 particles/mL		
		Run (n=3)	Average	SD	Run (n=3)	Average	SD
T=0	Media Bag	620	622	4	13	12	2
		619			13		
		627			9		
T=6 Hrs	Media Bag	77	73	6	6	4	3
		67			1		
		78			6		
T=12 Hrs	Media Bag	251	246	16	13	7	5
		229			6		
		259			3		
T=24 Hrs	Media Bag	31	24	8	0	0	0
		24			0		
		16			0		
T=30 Hrs	Media Bag	116	131	15	3	4	3
		146			7		
		130			1		

Table 8: HIAC results of CHS-1701 during 30 hours incubation in glass vial

Specifications: ≤ 6000 particles of ≥ 10 µm and ≤ 600 particles of ≥ 25 µm

Time point	Sample	≥ 10 µm particles/mL			≥ 25 particles/mL		
		Run (n=3)	Average	SD	Run (n=3)	Average	SD
T=0	Glass Vial	110	120	6	5	6	3
		123			9		
		126			4		
T=6 Hrs	Glass Vial	132	138	5	8	6	2
		142			6		
		139			5		
T=12 Hrs	Glass Vial	124	131	11	5	4	2
		144			5		
		126			2		
T=24 Hrs	Glass Vial	66	77	10	2	3	2
		84			2		
		82			5		
T=30 Hrs	Glass Vial	71	62	8	3	2	2
		55			0		
		59			4		

4. Conclusion

Results from the compatibility study of Coherus' CHS-1701 in its current formulation revealed that the product remained within Coherus' specifications during storage in either a sterile glass vial or a pre-sterilized HyClone BPC Media Bag for up to 30 hours at ambient temperature. Additionally, no significant changes were observed over time.

Samples acquired over 30 hours of storage in either a glass vial or media bag remained clear and without discoloration or visible particulates over 30 hours at ambient temperature. Product concentrations detected by A_{280} and A_{320} measurements over 30 hours at ambient temperature in either a glass vial or media bag and remained within method variability (±3%) and within Coherus' specifications of 10.0 ± 1.0 mg/mL.

Additionally, no significant changes in product stability were detected by SE-HPLC and RP-HPLC analyses over 30 hours at ambient temperature in either a glass vial or media bag. All samples showed SE-HPLC main peak percentages within method variability (Main Peak RSD ≤<0.2%) and within Coherus' specifications of ≥ 95.0% and RP-HPLC main peak percentages within method variability (Main Peak RSD ≤ 0.2%) and within Coherus' specifications of ≥ 90.0%.

Furthermore, HIAC results revealed no significant differences in subvisible particle concentrations as a result of storage in either a glass vial or media bag, or over time for up to 30 hours at ambient temperature. All samples, regardless of incubation time or container closure system, resulted in values below the USP <788> specifications for both 10 µm and 25 µm bin sizes.

Overall, CHS-1701 in its current formulation showed no significant changes in stability as a result of storage in either a glass vial or media bag, or over time for up to 30 hours at ambient temperature, and remained within Coherus' specifications.

5. Appendix I. Study Design

August 27, 2015

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Study Design:
Compatibility Examination for CHS-1701

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1. Study Design

Purpose:	Study guidelines for the execution of Coherus's compatibility study for CHS-1701, per contract signed between Coherus and Integrity Bio, Inc. (IBI).

1.1 General information

Client:	Coherus
Product:	CHS-1701: Pegfilgrastim (PEGylated recombinant human granulocyte colony-stimulating factor (GCSF))
Study Title:	Compatibility Examination for CHS-1701
Study Objective:	To assess the the stability of Pegfilgrastim when stored in representative vessels (both glass and bag) over a 30 hour period.
Names of investigators:	Byeong Chang, Ph.D., Mark Hokenson, Ph.D., Hana Chang, Ph.D., Trevers Bennett, Richard Redman, David Agdaian and Jamie Spahn
Expected Timeline:	Approx. 2 weeks

1.2 Analytical and Testing Methods

Coherus' analytical methods to be employed for this examination (previously transferred to Integrity Bio, Inc.):

- Size Exclusion HPLC (SE-HPLC); document no. AM.AL.0028.00 (revision 00)
- Reversed-Phase HPLC (RP-HPLC); document no. AM.AL.0033.00 (revision 00)
- Spectrophotometry (protein concentration by A_{280}): Eurofins document no. 1-P-QM-WI -9020609_04 (revision 04)

In addition to the product-specific analytical methods mentioned above, IBI will also utilize the following standard methods for analyzing the GCSF product:

- Visual inspection (for color, appearance and clarity)
- HIAC (5 mL method, via 1 mL sips)

Finally, sample aliquots will also be shipped out to a third party laboratory (ELLI) for bioassay analysis.

1.3 Materials

1.3.1 Pegfilgrastim Drug Product (DP)

DP Presentation:	Liquid material
DP Concentration:	10 mg/mL
DP Formulation:	10 mM sodium acetate, 5% sorbitol and 0.004% P20, pH 4.0
DP Volume:	~250 mL
Storage Temperature:	2-8°C
DP Lot number:	TBD

1.3.2 Materials and Preparation

Media Bag Container:	Pre-sterilized HyClone BPC Pyrex®, TC Tech Media bag, 100 mL (P/N SH3B6501)
Glass Container:	Pyrex® Media borosilicate glass vial, Corning®, 100 mL
Filters:	0.22 µm PVDF vacuum filter system (Agros BVP2225)
Filling:	The autoclaved Pyrex® vial and the pre-sterilized media bad will be filled with the sterile-filtered drug product under aseptic conditions using a biological safety cabinet (BSC).
Fill volume:	90 mL

1.4 Pegfilgrastim Compatibility Study

In this evaluation, the compatibility of CHS-1701 (containing 10 mg/mL Pegfilgrastim, 10 mM sodium acetate, 5% sorbitol and 0.004% polysorbate 20, pH 4.0) will be assessed with the following representative vessels over time at ambient storage conditions:

- Glass (formulation vessel); small Pyrex® vial
- Media bag; small Hyclone BioProcess container (TC Tech media bag)

NOTE – these studies will *not* include the compatibility assessment of CHS-1701 with platinum cured silicone (transient contact), Teflon gasket (on filling nozzle) and stainless steel (nozzle).

1.4.1 Preparation for Analysis

The CHS-1701 drug product (DP) will be sterilize filtered and filled into both the autoclaved glass and pre-sterilized bag containers. This process will be performed in a biological safety cabinet (BSC) to ensure sterility. The sterile-filtered DP will be filled at a volume of 90 mL, for both vessels. No inversion of the bag or glass vials will be performed after filling. After filling, the containers will be sealed.

1.4.2 Storage Conditions and Analysis

The CHS-1701 DP, in both the Pyrex® glass and Media bag containers, will be stored at ambient conditions (~23°C) under fluorescent light in the BSC. At varying time points during storage, alqiouts will be aseptically removed from each container for analysis. Aliquot removal will be performed in a BSC to maintain the sterility of the samples in the containers. Table 1 shows the analysis time points for this study.

Table 1. Conditions for the CHS-1701 Compatibility Evaluation

Vessels	Time Point(s)
Glass	0, 6, 12, 24 and 30 hours
Bag	6, 12, 24 and 30 hours

A total of 7 mL will be aseptically removed at each time point and immediate analysis at each sampling time point will be conducted. Each sample aliquot will be immediately analyzed by visual inspection (photographs of the aliquots will be acquired), A_{280}, SE-HPLC, RP-HPLC and HIAC.

1.4.3 Acceptance Criteria

The acceptance criteria of the various assays employed to analyze CHS-1701 in this study are detailed in Table 2.

Table 2. Acceptance Criteria for CHS-1701 Methods

Assay	Specification	Method Variability
A280/Protein Concentration	10.0 ± 1.0 mg/mL	+/- 3%
SE-HPLC	Main Peak ≥ 95.0%	Main Peak RSD <0.2%
RP-HPLC	Main Peak ≥ 90.0%	Main Peak RSD ≤ 0.2%
HIAC	≤ 6000 particles of ≥ 10 µm ≤ 600 particles of ≥ 25 µm	N/A
Visual Inspection	Essentially free of visible particulates	N/A

2. Reporting

Within 1-2 weeks after completing the final time point, data will be summarized in PowerPoint slides and ChemStation PDF reports and presented to the Coherus team. A final report will also be drafted following the conclusion of the study.