CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761082Orig1s000

CLINICAL PHARMACOLOGY REVIEW(S)

Office of Clinical Pharmacology
351(k) Biosimilar Review

351(k) BLA Number	761082
Applicant	Adello Biosciences, LLC
Submission Date	July 8, 2017
Submission Type	*Standard*
Link to EDR	\\CDSESUB1\evsprod\BLA761082\
Proprietary Name (Proposed) / Nonproprietary Names	Releuko / theragrastim[1], filgrastim-ayow
Dosage Form and Strength	300 mcg/mL and 480 mcg/1.6 mL in single-dose vials; 300 mcg/0.5 mL and 480 mcg/0.8 mL in single-dose prefilled syringes
Route of Administration	*Subcutaneous (SC)injection or Intravenous (IV) infusion*
Proposed Indication(s)	• *Decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti- cancer drugs associated with a significant incidence of severe neutropenia with fever.* • *Reduce the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML)* • *Reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation (BMT).* • *Reduce the incidence and duration of sequelae of severe neutropenia, (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.*
Associated IND	*115333*
Reference Product Information (U.S.-licensed)	
Proprietary (Non-Proprietary) Name	Neupogen (filgrastim)
Dosage Form and Strength	300 mcg/mL and 480 mcg/1.6 mL in single-dose vials; 300 mcg/0.5 mL and 480 mcg/0.8 mL in single-dose prefilled syringes
OCP Review Team Signers	
OCP Review Team	*Xianhua (Walt) Cao, PhD* *Sarah J. Schrieber, PharmD*
OCP Final Signatory	*Nam Atiqur Rahman, PhD*

[1] In this document, we generally refer to the applicant's proposed product by the applicant-provided descriptor "theragrastim", which was the name used to refer to this product during development. Subsequently, the nonproprietary name for this proposed product has been conditionally accepted to be "filgrastim-ayow."

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1. EXECUTIVE SUMMARY

This Biologic License Application (BLA) for RELEUKO (filgrastim-ayow), a recombinant methionyl human granulocyte colony stimulating factor (G-CSF), has been submitted under Section 351(k) of the Public Health Service Act (42 U.S.C. 262(k)). The applicant is seeking approval for RELEUKO (filgrastim-ayow), referred to as "theragrastim" by the applicant during development and herein, as a proposed biosimilar to US-licensed Neupogen (filgrastim) licensed under BLA 103353 by Amgen Inc. The applicant is seeking licensure only for the neutropenia indication for which US-licensed Neupogen is currently approved. The applicantion included pharmacokinetic (PK), pharmacodynamics (PD), immunogenicity data to support a demonstration of no clinical meaningful differences between theragrastim and US-licensed Neupogen in terms of safety, purity, and potency. The PK/PD similarity study TPI-CL-106 and the immunogenicity study TPI-CL-106-110 were conducted in healthy subjects comparing theragrastim and US-licensed Neupogen.

Study TPI-CL-106 was a single-dose, randomized, double-blind, 2-period crossover study in 58 healthy subjects designed to determine the PK and PD (absolute neutrophil count (ANC)) similarity of theragrastim and US-licensed Neupogen following a single 5 μg/kg subcutaneous (SC) dose. The 90% confidence intervals (CI) for comparisons of the PK and PD endpoints were within the limits of 80 to 125%. The results of the study established the PK and PD similarity between theragrastim and US-licensed Neupogen based on the primary PK endpoints of C_{max} and $AUC_{0\text{-}inf}$ and PD endpoints of ANC_{max} and ANC $AUEC_{last}$.

The incidence of anti-drug antibodies (ADAs) was compared in Study TPI-CL-110, a randomized, multiple-dose, parallel study in 134 healthy subjects. The results indicate no treatment emergent ADA for either theragrastim or US-licensed Neupogen. The assessment of the impact of ADA on PK, PD, and safety are limited due to no subjects with treatment emergent ADA, and no PK sampling. The data indicates that there is no increase in immunogenicity risk for theragrastim as compared to US-licensed Neupogen.

In conclusion, the PK, PD (ANC), and immunogenicity results support a demonstration of no clinically meaningful differences between theragrastim and US-licensed Neupogen and add to the totality of the evidence to support a demonstration of biosimilarity of theragrastim and US-licensed Neupogen.

1.1 Recommendations

The Office of Clinical Pharmacology recommends approval of theragrastim based on demonstration of PK and PD similarity and no increase in immunogenicity risk between theragrastim and US-licensed Neupogen.

Review Issue	Recommendations and Comments
Pivotal evidence of PK similarity	In study TPI-CL-106, PK similarity was demonstrated between theragrastim and US-licensed Neupogen. The 90% CI of the geometric mean ratio for the primary PK endpoints of C_{max} and AUC_{inf} fell within the margin of 80-125%.

Pivotal evidence of PD similarity	In study TPI-CL-106, PD (ANC) similarity was demonstrated between theragrastim and US-licensed Neupogen. The 90% CI of the geometric mean ratio for the primary PD endpoints of ANC_{max} and ANC $AUEC_{last}$ fell within the margin of 80-125%.
Evidence of immunogenicity comparability	The results of Study TPI-CL-110 indicate similar incidence of ADA for theragrastim and US-licensed Neupogen.

1.2 Post-Marketing Requirements and Commitments

None

2. SUMMARY OF CLINICAL PHARMACOLOGY ASSESSMENT

2.1 Clinical Pharmacology and Pharmacokinetics

Theragrastim is a proposed biosimilar to US-licensed Neupogen. US-licensed Neupogen (filgrastim) is a recombinant methionyl human G-CSF (filgrastim). Details on the clinical pharmacology of US-licensed Neupogen can be found in the product label (USPI).

In Study TPI-CL-106, the 90% CI for the geometric mean ratios of the primary PK endpoints of C_{max} and $AUC_{0\text{-}inf}$ and the primary PD endpoints of ANC_{max} and ANC $AUEC_{last}$ were within the limits of 80% to 125% between theragrastim and US-licensed Neupogen, as summarized in **Table 1**.

Table 1. Summary of Statistical analyses for assessment of PK and PD (ANC) similarity (Study TPI-CL-106)

Comparison	**Geometric Mean Ratio* (90% CI)**			
	PK Endpoints		**PD Endpoints**	
	C_{max}	**$AUC_{0\text{-}inf}$**	**ANC_{max}**	**ANC $AUEC_{last}$**
Theragrastim vs US-licensed Neupogen	89.2 (83.3-95.5)	90.7 (85.1-96.7)	104 (100.4-107.6)	101.8 (98.6-105.2)

*Presented as percent

Overall, the submitted clinical pharmacology studies adequately demonstrate similarity of PK and PD (ANC), supporting a finding of no clinically meaningful differences and adding to the totality of the evidence to support a demonstration of biosimilarity of theragrastim and US-licensed Neupogen.

The incidence of ADAs was compared in Study TPI-CL-110, a comparative clinical study between theragrastim and US-licensed Neupogen in healthy subjects. The results of the study indicate no subjects with treatment-emergent anti-drug antibodies (ADAs) for theragrastim and US-licensed Neupogen. The assessment of the impact of ADA on PK, PD, and safety is limited due to no treatment-emergent ADA, and no PK sampling. The data indicates that there is no increase in immunogenicity risk for theragrastim as compared to US-licensed Neupogen, and supports the demonstration of no clinically meaningful differences between theragrastim and US-licensed Neupogen.

2.2 Outstanding Issues

None

3. COMPREHENSIVE CLINICAL PHARMACOLOGY REVIEW

3.1 Regulatory Background

3.1.1 Describe relevant regulatory history for the review of this 351(k) BLA.

Theragrastim is a proposed biosimilar to US-licensed Neupogen. The applicant is seeking the neutropenia related indications:

- Decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.
- Reduce the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML)
- Reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation (BMT).
- Reduce the incidence and duration of sequelae of severe neutropenia, (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.

The applicant is not seeking approval for the following indications:

- To mobilize autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.
- To increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome).

3.2 Clinical Pharmacology Review Questions

3.2.1 What are the design features of the clinical pharmacology and/or clinical studies to support biosimilarity?

The applicant conducted one pivotal PK/PD similarity study and one comparative immunogenicity study as described in **Table 2**.

Table 2. Summary of Relevant Theragrastim Clinical Studies

Protocol	Title	Subjects	Objectives	Route/Dose/Duration
PK/PD Similarity Study				
TPI-CL-106 (Pivotal)	A Randomized, Comparative Pharmacokinetic /Pharmacodynamics, Double-Blind, Single-Dose, Two-Period Crossover Study Comparing Theragrastim to Neupogen in Healthy Subjects	Healthy (N=58)	PK, PD (ANC), safety	5 µg/kg SC single dose of Theragrastim vs. US-licensed Neupogen

Immunogenicity Study				
TPI-CL-110	A Randomized, Single-Blind Study Comparing Safety and Immunogenicity Between Theragrastim and Neupogen in Healthy Adult Subjects	Healthy (N=134)	Safety & immunogenicity	5 µg/kg SC, daily for 5 days (day 1-day 5) at cycle 1, and a single dose on day 33 (cycle 2) of Theragrastim vs. US-licensed Neupogen

Study TPI-CL-106 provided pivotal evidence to support PK and PD (ANC) similarity. This study was a single-dose, randomized, double-blind, 2-treatment crossover study designed to compare the PK and PD (ANC) profiles of between theragrastim and US-licensed Neupogen administered as a single 5 µg/kg subcutaneous (SC) dose to healthy subjects (N=58). The PK endpoints were C_{max} and $AUC_{0\text{-}inf}$ and the PD endpoints were ANC_{max} and ANC $AUEC_{last}$. PK and PD similarity was concluded if the 90% CI of the geometric mean ratios between theragrastim and US-licensed Neupogen were within the limits of 80% to 125%.

The study design of Study TPI-CL-106 is considered adequate due to the following reasons:

1. A cross-over study design is recommended for products with short half-life and the PD (ANC) response is rapid.
2. A study in healthy subjects is considered safe and more sensitive compared with that in patients with potentially confounding factors such as underlying disease, concomitant medications, and other factors.
3. Considering PK assay sensitivity, dose-exposure linearity, and tolerability, a single SC dose of 5 µg/kg is considered acceptable.
4. The at least 14-day washout between treatment periods was adequate. Serum G-CSF concentrations were below the lower limit of quantitation (LLOQ) by 36 hours post-dose after each treatment period, and ANC had returned to baseline by around 72 hours after each treatment as well.

Study TPI-CL-110 was a single center, single-blind, randomized, multiple-dose, parallel-arm study in 134 healthy subjects evaluating the incidence of immunogenicity of theragrastim and US-licensed Neupogen administered 5 µg/kg SC daily for 5 days (Cycle 1, Days 1 – 5) followed by a single 5 µg/kg SC dose on Day 33 (Cycle 2, Day 1). There was a 28 days washout period between the fifth dose on Cycle 1, Day 5 and the single dose on study day 33 (Cycle 2, Day 1). The results indicate no subjects with treatment emergent anti-drug antibodies (ADA) for both products.

The data from the PK/PD similarity and immunogenicity studies supports the demonstration of no clinically meaningful differences between theragrastim and US-licensed Neupogen.

3.2.2 What are the endpoints in the clinical pharmacology and/or clinical studies to support biosimilarity?

In Study TPI-CL-106 the PK similarity criteria for C_{max} and $AUC_{0\text{-}inf}$ were that the 90% CI of the geometric mean ratio should lie within 80-125%. This margin proposed by the applicant was acceptable. The pre-specified PD (ANC) similarity criteria for maximum ANC count (ANC_{max}) and area under the

effect curve (ANC $AUEC_{last}$) were that the 90% CI of the geometric mean ratio should lie within 80 - 125%.

- PK serum samples were collected on Day 1 at pre-dose, 0.5, 0.75, 1, 1.5, 2, 3, 4, 5, 6, 8, 10, 12, 16, 24, and 36 hours post-dose.
- PD (ANC) serum samples were collected at pre-dose, 0.5, 1, 2, 4, 6, 8, 10, 12, 16, 20, 24, 32, 48, and 72 hours post-dose.

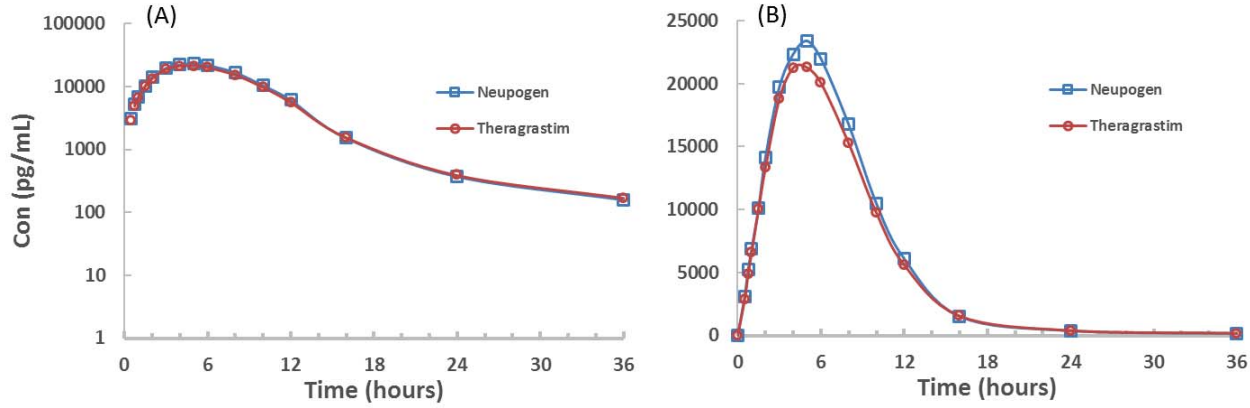
3.2.3 Are the pharmacologically active moieties of the proposed biosimilar and the reference product in plasma (or other biological matrix) appropriately identified and measured to assess the PK parameters?

Yes. See **Section 4.1** for details. G-CSF levels were measured in serum by a validated enzyme-linked immunosorbent assay (ELISA). Absolute neutrophil counts (ANC) were determined using an appropriate hematology analyzer.

3.2.4 Is PK similarity met?

Yes, PK similarity between theragrastim and US-licensed Neupogen was demonstrated, where the 90% CIs of geometric mean ratios of PK endpoints for each product pairwise comparison were contained within prospectively defined criteria of 80 to 125% (**Table 1**). The geometric mean G-CSF concentration-time profiles are shown in **Figure 1.** A summary of the 5 µg/kg SC single dose PK parameters from Study TPI-CL-106 for each product is shown in **Table 3**.

Figure 1. Geometric mean serum G-CSF concentration vs. time profile (Study TPI-CL-106)



(A) concentrations in logarithmic scale, (B) concentrations in linear scale.

Table 3. Summary of PK parameters (Study TPI-CL-106)

PK parameters	Geometric Mean (% CV)	
	Theragrastim (n=53[c])	US-licensed Neupogen (n=53)
C_{max} (ng/mL)	21.8 (42)	24.3 (28)
AUC_{0-t} (ng/mL*hr)	184 (35)	201 (27)
AUC_{0-inf} (ng/mL*hr)	186 (34)	202 (27)
T_{max} (hr)[a]	5.0 (3, 10)	5.0 (3, 8)

$T_{1/2\_el}$ (hr) [b]	6.3 ± 2.6	5.8 ± 1.9

% CV: coefficient of variation, $T_{1/2\_el}$: terminal half-time, [a]presented as median (minimum, maximum), [b]presented as arithmetic mean ± standard deviation, [c]n=54 subjects completed the study but one subject was excluded from the analysis due to incomplete dosing in Period 1

3.2.5 Is PD similarity met?

Yes, PD (ANC) similarity between theragrastim and US-licensed Neupogen was demonstrated, where the 90% CIs of geometric mean ratios of PD endpoints were contained within prospectively defined criteria of 80 to 125%. (**Table 1**). The PD time profiles and the summary of PD parameters from Study TPI-CL-106 for each product are shown in **Figure 2** and **Table 4**.

Figure 2. Geometric mean ANC vs. time profile (Study TPI-CL-106)

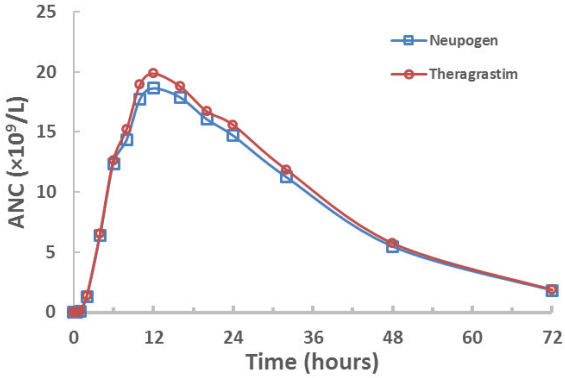


Table 4. Summary of PD parameters (Study TPI-CL-106)

PK parameters	Geometric Mean (%CV)	
	Theragrastim (n=53)	US-licensed Neupogen (n=53)
ANC_{max} (10^9/L)	19.8 (23.5)	18.6 (25.1)
ANC $AUEC_{last}$ (h*10^9/L)	668 (20.6)	617 (33.0)

% CV: coefficient of variation

Immunogenicity

3.2.6 Is the immunogenicity assay capable of detecting the antidrug antibodies (ADA) in the presence of concentration of product in the study samples?

Yes. The sensitivity of the ADA assay was 65.3 ng/ml for anti-G-CSF. The low and high positive controls were 100 ng/ml and 1600 ng/ml, respectively. The drug tolerance of the ADA assay was 39.1 ng/ml for anti-G-CSF. Refer to the immunogenicity assay review by the Office of Biological Products review team for details regarding the assays.

3.2.7 Is the sampling plan adequate to capture baseline, early onset, and dynamic profile (transient or persistent) of anti-drug antibodies (ADA) formation?

Yes. The sampling schedules in the studies were appropriate to minimize interference from the presence of the product in the samples, if the ADA assay is not drug-tolerant. The sampling schedule for Study TPI-CL-110 was on

- Cyle 1, Day 1 (baseline), 8, and 22
- Cycle 2, Day 21 (i.e., study day 54).

3.2.8 What is the incidence of anti-drug antibodies (ADA)? (Provide the incidence of pre-existing antibodies at baseline and the incidence of ADA throughout the study.)

Study TPI-CL-110 was a randomized, multiple-dose, parallel study in 134 healthy subjects. Subjects were randomized to either theragrastim or US-licensed Neupogen administered 5 µg/kg SC daily for 5 days (Cycle 1, Days 1 – 5) followed by a single 5 µg/kg SC dose on Day 33 (Cycle 2, Day 1). There was a 28 days washout period between the fifth dose on Cycle 1, Day 5 and the single dose on study day 33 (Cycle 2, Day 1). Six subjects were discontinued due to earlier non-compliance or personal reasons.

Summary of the incidence of ADA in Study TPI-CL-110 is shown in **Table 5**. One subject randomized to the theragrastim arm tested ADA positive at baseline and remained ADA positive post-dose on Day 8 but tested negative for ADA on Day 22 post-dose. Given this subject was ADA positive at baseline, this subject is not considered as having treatment emergent ADA. Thus, no neutralized assay was conducted in this study.

Table 5. Immunogenicity results for binding ADA in Study TPI-CL-110

	N	Anti-G-CSF	
		Baseline	**Treatment-emergent**
Theragrastim	67	1/67 (1.5%)	0/65 (0%)
US-licensed Neupogen	67	0/67 (0%)	0/67 (0%)

3.2.9 Do the anti-drug antibodies (ADA) have neutralizing activity?

In Study TPI-CL-110, no neutralizing assay was conducted. See **Section 3.2.8**.

3.2.10 What is the impact of anti-drug antibodies (ADA) on the PK, PD, efficacy, and safety of the therapeutic protein?

The impact of ADA on PK cannot be assessed as no subjects in Study TPI-CL-110 indicated positive treatment-emergent ADA. In addition, there were no PK samples were collected in Study TPI-CL-110. With the low incidence rate of the ADA, it is unlikely to have any impact on the PK, PD, efficacy or safety from the ADA.

4. APPENDICES

4.1 Summary of Bioanalytical Method Validation and Performance

4.1.1 Pharmacokinetics

4.1.1.1 How are the concentrations of the pharmacologically active moieties (parent and/or any relevant catabolites) measured in the plasma and other matrices in the clinical pharmacology studies?

Serum G-CSF concentrations were determined using a validated Enzyme-Linked Immunosorbent Assay (ELISA) procedure with a Human G-CSF DuoSet ®Kit from R&D Systems. The method for the quantification of theragrastim and US-licensed Neupogen in human serum was validated at (b) (4) (Report # 6849033111). A partial validation was subsequently performed by (b) (4) (Report# 7896032814) to qualify the method to use in quantification of theragrastim and US-licensed Neupogen over the concentration range studied (70-5000 pg/mL). Serum G-CSF was measured using a validated sandwich ELISA in which mouse anti-human G-CSF Mab was used as capture reagents and biotinylated polyclonal anti-human G-CSF antibodies, and streptavidin HRP were used as detection reagents (Validation reports 6849033111 and 7896032814). Standard calibrators were prepared by spiking WHO G-CSF in 100% serum. The validation reports and bioanalytical study report (Report # 8817033015) for study TPI-101-106 were reviewed. A summary of the ELISA validation and in-study performance for theragrastim and US-licensed Neupogen are show in **Table 6.**

Table 6. Summary of theragrastim and US-licensed Neupogen Assay Validation Reports

Analyte	**Theragrastim**	**US-Licensed Neupogen**
Matrix	Human Serum	
Test Products	Lot# 40-13013	Lot# 1028686 and 1026690
Reference G-CSF standard	WHO/NIBSC Part# 09/136 (1000 ng dry powder per vial)	
Dilution Factor	0.05	
Standard curve concentrations (pg/mL)	39 (anchor), 70 (LLOQ), 156, 313, 625, 1250, 2500, 5000 (ULOQ)	
LLOQ	70 pg/ml	
ULOQ	5000 pg/ml	
Method Validation Summary		
Standard curve accuracy (%Bias) from 70 to 5000 pg/ml	-0.8 to 2.0	
Inter-assay Precision: %CV	LLOQ (70 pg/ml): 5.6 Low (210 pg/ml): 5.7 Mid (625 pg/ml): 5.7 High (3750 pg/ml): 11.2 ULOQ (5000 pg/ml): 15.4	LLOQ (70 pg/ml): 6.0 Low (210 pg/ml): 6.4 Mid (625 pg/ml): 5.4 High (3750 pg/ml): 5.9 ULOQ (5000 pg/ml): 4.7
Inter-assay Accuracy: %Bias	LLOQ (70 pg/ml): 19.8 Low (210 pg/ml): 18.3 Mid (625 pg/ml): 17.6 High (3750 pg/ml): 13 ULOQ (5000 pg/ml): 8.9	LLOQ (70 pg/ml): 1.7 Low (210 pg/ml): 4.9 Mid (625 pg/ml): 5.8 High (3750 pg/ml): -0.3 ULOQ (5000 pg/ml): -2.8
Intra-assay Precision: %CV	LLOQ (70 pg/ml): 5.4 Low (210 pg/ml): 5.7	LLOQ (70 pg/ml): 5.0 Low (210 pg/ml): 5.4

	Mid (625 pg/ml): 5.4 High (3750 pg/ml): 4.1 ULOQ (5000 pg/ml): 8.4	Mid (625 pg/ml): 4.3 High (3750 pg/ml): 4.1 ULOQ (5000 pg/ml): 2.8
Intra-assay Accuracy: %Bias	LLOQ (70 pg/ml):19.8 Low (210 pg/ml): 18.3 Mid (625 pg/ml): 17.6 High (3750 pg/ml): 13 ULOQ (5000 pg/ml): 8.9	LLOQ (70 pg/ml): 1.7 Low (210 pg/ml): 4.9 Mid (625 pg/ml): 5.8 High (3750 pg/ml): -0.3 ULOQ (5000 pg/ml): -2.8
Hook effect	No hook effect observed	
Dilution linearity with acceptance criteria: %CV ≤ 20.0 and %RE ± 20.0	Up to a 667-fold dilution	up to a 100-fold dilution
Interference	No matrix effect	
Bench-top/process stability	Stable at room temperature for 21 hours and at 4°C for 27 hours in serum	
Freeze-thaw stability	Up to 4 cycles at -70°C; Up to 2 cycles at -20°C	
Frozen serum storage stability (days)	At nominal -20°C and -70°C for 104 days	
Method Performance for Study TPI-CL-101-106		
Assay passing rate	70 out of 75 runs (including incurred sample reanalysis (ISR)) met the method acceptance criteria.	
Standard curve performance	• Cumulative bias range: -6.41 to 4.79% • Cumulative precision: ≤ 7.87 %CV	
QC performance	• Cumulative bias range: -3.1 to 3.5% • Cumulative precision: ≤ 13.4 %CV • TE: ≤ 16.89%	
Method reproducibility	• Incurred sample reanalysis was performed in 2.5% of study samples and 90.7% of samples met the pre-specified criteria	
Study sample stability	• Analyzed within 54 days from collection (within established stability	

4.1.2 Pharmacodynamics

4.1.2.1 What bioanalytical methods were used to assess the pharmacodynamic (PD) biomarker(s) and/or the PD effect(s) of the biologic?

Absolute neutrophil count (ANC) was determined with an Sysmex XE2100 Hematology analyzer by (b) (4) using a validated hematology method as cleared by FDA for diagnostic use and detailed in (b) (4) Standard Operating Procedures (SOPs). All assays were validated and reports were submitted.

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/s/

XIANHUA W CAO
04/04/2018

SARAH J SCHRIEBER
04/04/2018

NAM ATIQUR RAHMAN
04/04/2018
I agree with the recommendation.