IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF WEST VIRGINIA
CLARKSBURG DIVISION

REGENERON PHARMACEUTICALS, INC., *Plaintiff*, v. CELLTRION, INC., *Defendant*.	Civil Action No. 1:23-cv-89-TSK **CONFIDENTIAL** **FILED UNDER SEAL**
REGENERON PHARMACEUTICALS, INC., *Plaintiff*, v. SAMSUNG BIOEPIS, CO., LTD., *Defendant*.	Civil Action No. 1:23-cv-94-TSK **CONFIDENTIAL** **FILED UNDER SEAL**
REGENERON PHARMACEUTICALS, INC., *Plaintiff*, v. SAMSUNG BIOEPIS, CO., LTD., *Defendant*.	Civil Action No. 1:23-cv-106-TSK **CONFIDENTIAL** **FILED UNDER SEAL**
REGENERON PHARMACEUTICALS, INC., *Plaintiff*, v. FORMYCON AG, *Defendant*.	Civil Action No. 1:23-cv-97-TSK **CONFIDENTIAL** **FILED UNDER SEAL**

DECLARATION OF KENNETH S. GRAHAM, PH.D.

I declare under penalty of perjury that the following is true and accurate to the best of my knowledge.

Dated: April 18, 2024

Kenneth S. Graham

Kenneth S. Graham, Ph.D.

1. I am Executive Director of Formulation Development at Regeneron Pharmaceuticals, Inc. ("Regeneron"). I am proud to have been an employee of Regeneron for over 22 years. During that time, I contributed to the development of formulations of VEGF Trap molecules, including the product which is now known as EYLEA.

2. I joined Regeneron's Formulation Development group in 2005. At that time, the group was engaged in stability studies for formulations of aflibercept. In these studies, we made formulations of aflibercept and subjected them to various stresses or storage conditions in order to analyze their stability. Part of my role in Formulation Development at this time was to conduct and oversee these stability studies.

3. When I joined Formulation Development in 2005, several years of research had already been conducted on aflibercept formulations at Regeneron. After I joined Formulation Development, I reviewed documentation concerning prior stability studies involving formulations for treating cancer and for ophthalmic use.

4. I am a named inventor of U.S. Patent 11,084,865 (Ex. 1). The'865 patent includes data from the "VGFT-SS207" study in Examples 3 and 4. SS207 evaluated a formulation containing 40 mg/ml VEGF Trap, 10 mM phosphate, 40 mM NaCl, 0.03% polysorbate 20, 5% sucrose, at pH 6.3.

5. I was the study director for SS207 and signed the study protocol on January 16, 2006. Ex. 2 (SS207 Protocol), RGN-EYLEA-BIOSIM-00710625. As study director, I ensured samples were pulled on schedule, managed staff, and analyzed and interpreted the study's experimental data, among other tasks.

6. The formulation tested in study SS207 is identified in the protocol as follows:

Test Article:

The basic composition of the formulation (lot # C2-5688-103-SPS) is:

10 mM Phosphate
40 mM NaCl
0.03% PS20
5 % Sucrose
40 mg/mL VEGF Trap
pH 6.25

Ex. 2 (SS207 Protocol), RGN-EYLEA-BIOSIM-00710618. The lot number of the formulation used in study SS207 is identified as C2-5688-103-SPS. (A "lot" refers generally to a batch or specific amount of a drug produced at a given time.) The VEGF Trap for this formulation lot came from VEGF Trap drug substance batch C05002M440, as identified in Regeneron's lab notebook 5688 issued to Megan Malone, an excerpt of which is attached as Exhibit 3. Ex. 3, RGN-EYLEA-BIOSIM-00474493-494.

7. SS207 evaluated this formulation in several different container systems. The Protocol identifies Device # 7 as 2 mL glass vials, to which I have added highlighting for clarity:

Table 1.

Device #	Glass barrel	Siliconization	Plunger	Closure Part
# 1	1 ml-l luer cone (OVS 10.6)	1000 cSt. silicone oil, spray siliconization	HV FM457 (V01311 or V00951)	HV FM27
# 2	1 ml-l luer cone (OVS 10.6)	1000 cSt. silicone oil, spray siliconization	West 4432/50 (V00916)	West 4023/50
# 3	1 ml-l luer cone (OVS 10.6)	1000 cSt. silicone oil, spray siliconization	West 4023/50, fluorotech (V00633)	West 4023/50
# 4	1ml-l staked needle **27 G**	1000 cSt. silicone oil, spray siliconization	West 4432/50 (V00916)	RNS FM27
# 5	1ml-l staked needle **27 G**	1000 cSt. silicone oil, spray siliconization	West 4023/50, fluorotech (V00633)	RNS FM27
# 6	1 ml-l luer cone (OVS 10.6)	Silicone emulsion, spray siliconization + heat tunnel	HV FM457 (V01311 or V00951)	HV FM27
# 7	2 mL glass vials	Not applicable	Not applicable	West Grey butyl rubber stopper 1888

Ex. 2 (SS207 Protocol), RGN-EYLEA-BIOSIM-00710619.

8. Size exclusion chromatography, or "SEC," was one of the tests performed on the formulation in SS207. As the protocol explains, size exclusion chromatography may be used to "detect and quantify molecular weight variants of VEGF Trap present in the stability samples." Ex. 2 (SS207 Protocol), RGN-EYLEA-BIOSIM-00710623.

9. Formulation Development maintained SEC data in excel spreadsheets. RGN-EYLEA-BIOSIM-00476242, attached as Ex. 4 after PDF conversion, is an excel file with the file name "VGFT-SS207 SEC." As its name suggests, this file includes SEC data from SS207. The "5C" sheet in the spreadsheet contains the SEC data for the vials (Device #7) stored at 5°C. One column in the spreadsheet is "% Native VEGF-TRAP." In the '865 patent, the "% Native VEGF-TRAP" data from the spreadsheet is referred to as "% VEGF Trap Native Configuration." This data in the spreadsheet is the same as reported in the patent, except that the patent reports

the data with rounding to one fewer decimal place. The following comparison of the data illustrates this:

Time (months)	RGN-EYLEA-BIOSIM-00476242, "% Native VEGF-TRAP"	'865 Patent, Table 3, "% VEGF Trap Native Configuration"
0	99.49	99.5
0.5	99.42	99.4
1	99.49	99.5
2	99.18	99.2

10. SS207 was not the first time this formulation was evaluated. Several months earlier, in 2005, Formulation Development evaluated a formulation containing the same ingredients and amounts in Stability Study 195 ("SS195"). The protocol for SS195 is included in lab notebook 6223 of my former colleague and co-inventor on the '865 patent, Dr. Kelly Frye. An excerpt of this notebook is attached as Exhibit 5. Ex. 5, RGN-EYLEA-BIOSIM-00477402. Dr. Frye signed the protocol on October 10, 2005. The formulation for the study is identified as follows, with highlighting added to the row for Formulation #2:

Procedure:

The basic formulation for each formulation is

10 mM Phosphate
0.03% Polysorbate 20
40 mg/mL VEGF Trap
pH 6.25

Each formulation will have the following modifications:

Formulation #	Lot #	[NaCl] (mM)	[Sucrose] (%)	PEG 3350	Density (g/mL)
1	L05-255	40	5	0.1	1.031
2	L05-256	40	5	-	1.031
3	L05-257	0	7	0.1	1.038
4	L05-258	0	7	-	1.038
5	L05-259	135	-	0.1	1.011

Where PS 20 is polysorbate 20.

The listed ingredients in Formulation #2 are identical to the formulation evaluated in SS207, except that it involves formulation Lot # L05-256. The lab notebook several pages later identifies the drug substance (VEGF Trap) lot number for this formulation as FD050615P/Regn:

F2: lot # L05-256 density = 1.031 g/mL

Mfr. / Lot#	Reagent	Theoretical	Actual
	WFI	1.5309g	1.53g
JD-7147-02/Regn	100mM Phosphate	0.2648g	0.27g
JD-7147-05/Regn	300mM NaCl	0.5867g	0.59g
B07H10/Mallinckrodt	Sucrose	0.22g	0.2202g
JD-7147-04/Regn	1% polysorbate 20	0.132g	132µL
FD050615P/Regn	100.43mg/mL VEGF Trap	1.802g (1.752mL)	1.80g
	final wgt.	4.5364g	

RGN-EYLEA-BIOSIM-00477404. That is a different lot of aflibercept than was used in the SS207 study discussed above and set forth in the patent's Examples.

11. In stability study SS195, Regeneron evaluated Formulation #2 by SEC. The SEC data is reported in the excel file "pres VGFT-SS195 SEC," attached after PDF conversion as Exhibit 6. Ex. 6, RGN-EYLEA-BIOSIM-00474279. Like the SEC data file for SS207, the SEC data file for SS195 has a column for "% Native VEGF-TRAP," which means the same thing as it does in the SS207 SEC file, discussed above. While the SS195 Formulation #2 has the same ingredients and amounts as the formulation tested in SS207, the SEC data are somewhat different and generally show a lower level of % Native VEGF-TRAP. For example, the time zero data point for Formulation #2 for the 25°C storage condition shows 97.3% Native VEGF-TRAP, and the time zero data point for the 45°C storage condition shows 97.7% Native VEGF-TRAP. Each of the time zero SEC measurements for Formulation 2 are set forth below:

Experiment	% Native VEGF-Trap at T=0
45°C	97.7, 97.3
25°C	97.3, 97.6
37°C	97.7, 97.3
Freeze/Thaw	97.7
Vortex	97.7

Notably, the sample tested at the initiation of the experiment (time zero) does not undergo any storage at 25°C or 45°C or 5°C or any other elevated temperature and therefore reflects the % Native VEGF Trap at the time the formulation is prepared. My understanding is that the lower levels of % Native VEGF-TRAP (percent native configuration) reported in SS195 reflect the different lot of aflibercept used, which likely had a somewhat lower level of native VEGF-Trap as compared to the lot of aflibercept used in the formulation tested in SS207. That is consistent with my experience formulating VEGF Trap from various lots, as a fusion protein made in a biological system can exhibit somewhat higher or lower levels of % Native VEGF-Trap from lot to lot. Both VEGF Trap lots were made in CHO cells and were glycosylated.

Graham Ex. 1

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THE UNITED STATES OF AMERICA

TO ALL TO WHOM THESE PRESENTS SHALL COME:
UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office

July 22, 2022

THIS IS TO CERTIFY THAT ANNEXED HERETO IS A TRUE COPY FROM THE RECORDS OF THIS OFFICE OF:

PATENT NUMBER: *11,084,865*
ISSUE DATE: *August 10, 2021*

By Authority of the
Under Secretary of Commerce for Intellectual Property
and Director of the United States Patent and Trademark Office

Rodney Glover
Certifying Officer

US011084865B2

(12) **United States Patent**
Furfine et al.

(10) **Patent No.: US 11,084,865 B2**
(45) **Date of Patent: *Aug. 10, 2021**

(54) **VEGF ANTAGONIST FORMULATIONS SUITABLE FOR INTRAVITREAL ADMINISTRATION**

(71) Applicant: **REGENERON PHARMACEUTICALS, INC.**, Tarrytown, NY (US)

(72) Inventors: **Eric Furfine**, Concord, MA (US); **Daniel Dix**, LaGrangeville, NY (US); **Kenneth Graham**, Pleasant Valley, NY (US); **Kelly Frye**, Mendham, NJ (US)

(73) Assignee: **REGENERON PHARMACEUTICALS, INC.**, Tarrytown, NY (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **16/739,559**

(22) Filed: **Jan. 10, 2020**

(65) **Prior Publication Data**

US 2020/0131246 A1 Apr. 30, 2020

Related U.S. Application Data

(60) Continuation of application No. 16/582,486, filed on Sep. 25, 2019, which is a continuation of application No. 16/159,269, filed on Oct. 12, 2018, now Pat. No. 10,464,992, which is a continuation of application No. 15/879,294, filed on Jan. 24, 2018, now Pat. No. 10,400,025, which is a continuation of application No. 15/095,606, filed on Apr. 11, 2016, now Pat. No. 9,914,763, which is a continuation of application No. 14/330,096, filed on Jul. 14, 2014, now Pat. No. 9,340,594, which is a continuation of application No. 13/914,996, filed on Jun. 11, 2013, now Pat. No. 8,802,107, which is a continuation of application No. 13/329,770, filed on Dec. 19, 2011, now Pat. No. 8,481,046, which is a continuation of application No. 12/833,417, filed on Jul. 9, 2010, now Pat. No. 8,092,803, which is a continuation of application No. 12/560,885, filed on Sep. 16, 2009, now Pat. No. 7,807,164, which is a division of application No. 11/818,463, filed on Jun. 14, 2007, now Pat. No. 7,608,261.

(60) Provisional application No. 60/814,484, filed on Jun. 16, 2006.

(51) **Int. Cl.**

A61K 38/17	(2006.01)
A61K 38/18	(2006.01)
C07K 19/00	(2006.01)
C07K 14/71	(2006.01)
A61K 9/00	(2006.01)
A61K 9/19	(2006.01)
C07K 14/47	(2006.01)
A61M 5/178	(2006.01)
A61K 47/26	(2006.01)
A61K 47/02	(2006.01)
A61K 47/10	(2017.01)

(52) **U.S. Cl.**

CPC ***C07K 14/71*** (2013.01); ***A61K 9/0019*** (2013.01); ***A61K 9/0048*** (2013.01); ***A61K 9/19*** (2013.01); ***A61K 38/179*** (2013.01); ***A61K 38/1793*** (2013.01); ***A61K 47/02*** (2013.01); ***A61K 47/10*** (2013.01); ***A61K 47/26*** (2013.01); ***A61M 5/178*** (2013.01); ***C07K 14/47*** (2013.01); ***C07K 14/4705*** (2013.01); *C07K 2319/00* (2013.01); *C07K 2319/30* (2013.01)

(58) **Field of Classification Search**

None

See application file for complete search history.

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Primary Examiner — Christine J Saoud
Assistant Examiner — Jon M Lockard
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(57) **ABSTRACT**

Ophthalmic formulations of a vascular endothelial growth factor (VEGF)-specific fusion protein antagonist are provided suitable for intravitreal administration to the eye. The ophthalmic formulations include a stable liquid formulation and a lyophilizable formulation. Preferably, the protein antagonist has an amino acid sequence of SEQ ID NO:4.

64 Claims, No Drawings

Specification includes a Sequence Listing.

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VEGF ANTAGONIST FORMULATIONS SUITABLE FOR INTRAVITREAL ADMINISTRATION

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation application of U.S. patent application Ser. No. 16/582,486, filed on Sep. 25, 2019, which is a continuation application of U.S. patent application Ser. No. 16/159,269, filed on Oct. 12, 2018, which issued as U.S. Pat. No. 10,464,992 on Nov. 5, 2019, which is a continuation application of U.S. patent application Ser. No. 15/879,294, which issued as U.S. Pat. No. 10,400,025 on Sep. 2, 2013, filed on Jan. 24, 2018, which is a continuation application of U.S. patent application Ser. No. 15/095,606, filed on Apr. 11, 2016, which issued as U.S. Pat. No. 9,914,763 on Mar. 13, 2018, which is a continuation application of U.S. patent application Ser. No. 14/330,096, filed Jul. 14, 2014, which issued as U.S. Pat. No. 9,340,594 on May 17, 2016, which is a continuation of U.S. patent application Ser. No. 13/914,996, filed Jun. 11, 2013, which issued as U.S. Pat. No. 8,802,107 on Aug. 12, 2014, which is a continuation application of U.S. patent application Ser. No. 13/329,770, filed Dec. 19, 2011, which issued as U.S. Pat. No. 8,481,046 on Jul. 9, 2013, which is a continuation application of U.S. patent application Ser. No. 12/833,417, filed Jul. 9, 2010, which issued as U.S. Pat. No. 8,092,803 on Jan. 10, 2012, which is a continuation application of U.S. patent application Ser. No. 12/560,885, filed Sep. 16, 2009, which issued as U.S. Pat. No. 7,807,164 on Oct. 5, 2010, which is a divisional application of U.S. patent application Ser. No. 11/818,463, filed Jun. 14, 2007, which issued as U.S. Pat. No. 7,608,261 on Oct. 27, 2009, which claims the benefit under 35 U.S.C. .§ 119(e) of U.S. Provisional Application No. 60/814,484, filed Jun. 16, 2006, which applications are each hereby incorporated by reference.

BACKGROUND OF INVENTION

Field of the Invention

The present invention is directed to pharmaceutical formulations suitable for intravitreal administration comprising agents capable of inhibiting vascular endothelial growth factor (VEGF), and to methods for making and using such formulations. The invention includes liquid pharmaceutical formulations having increased stability, as well as formulations that may be lyophilize and reconstituted for intravitreal administration.

Statement of Related Art

Vascular endothelial growth factor (VEGF) expression is nearly ubiquitous in human cancer, consistent with its role as a key mediator of tumor neoangiogenesis. Blockade of VEGF function, by binding to the molecule or its VEGFR-2 receptor, inhibits growth of implanted tumor cells in multiple different xenograft models (see, for example, Gerber et al. (2000) Cancer Res. 60:6253-6258). A soluble VEGF-specific fusion protein antagonist, termed a "VEGF trap" has been described (Kim et al. (2002) Proc. Natl. Acad. Sci. USA 99:11399-404; Holash et al. (2002) Proc. Natl. Acad. Sci. USA 99:11393-8), which applications are specifically incorporated by reference in their entirety.

Ophthalmic formulations are known, see for example, U.S. Pat. Nos. 7,033,604 and 6,777,429. An ophthalmic formulation of a VEGF antibody is described in U.S. Pat. No. 6,676,941.

Lyophilization (freeze drying under controlled conditions) is commonly used for long-term storage of proteins. The lyophilized protein is substantially resistant to degradation, aggregation, oxidation, and other degenerative processes while in the freeze-dried state (see, for example, U.S. Pat. No. 6,436,897).

BRIEF SUMMARY OF THE INVENTION

Stable formulations of a VEGF-specific fusion protein antagonist are provided. Pharmaceutically acceptable formulations are provided that comprise a VEGF "trap" antagonist with a pharmaceutically acceptable carrier. In specific embodiments, liquid and lyophilized formulations are provided.

In a first aspect, a stable liquid ophthalmic formulation of a VEGF-specific fusion protein antagonist is provided, comprising a fusion protein that comprises a receptor component consisting essentially of an immunoglobulin-like (Ig) domain 2 of a first VEGF receptor and Ig domain 3 of a second VEGF receptor, and a multimerizing component (also termed a "VEGF trap"). In a specific embodiment of the VEGF-specific fusion protein antagonist, the first VEGF receptor is Flt1 and the second VEGF receptor is Flk1 or Flt4. In a more specific embodiment the fusion protein has the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4. Preferably, the VEGF antagonist is a dimer comprising two fusion proteins of SEQ ID NO:4.

In one aspect, a stable liquid ophthalmic formulation is provided that comprises 1-100 mg/ml VEGF-specific fusion protein antagonist, 0.01-5% of one or more organic co-solvent(s), 30-150 mM of one or more tonicity agent(s), 5-40 mM of a buffering agent, and optionally, 1.0-7.5% of a stabilizing agent, pH between about 5.8-7.0.

In one or more specific embodiments, the organic co-solvent may be polysorbate, for example, polysorbate 20 or polysorbate 80, polyethylene glycol (PEG), for example, PEG 3350, or propylene glycol, or a combination thereof; the tonicity agent may be, for example, sodium chloride or potassium chloride; the stabilizing agent may be sucrose, sorbitol, glycerol, trehalose, or mannitol; and the buffering agent may be, for example, phosphate buffer. In a specific embodiment, the phosphate buffer is a sodium phosphate buffer.

In various embodiments, the organic co-solvent is polysorbate and/or PEG, the stabilizing agent is sucrose, the buffering agent is phosphate buffer, and the tonicity agent is sodium chloride.

More specifically, the stable liquid ophthalmic formulation comprises about 40-50 mg/ml of the VEGF antagonist (SEQ ID NO:4), about 10 mM phosphate buffer, 0.01-3% polysorbate and/or PEG, 40-135 mM sodium chloride, and optionally 5.0% sucrose, pH about 6.2-6.3.

In a specific preferred embodiment, the stable liquid ophthalmic formulation comprises about 50 mg/ml of the VEGF antagonist (SEQ ID NO:4), 10 mM sodium phosphate buffer, 50 mM sodium chloride, 0.1% polysorbate, and 5% sucrose, pH about 6.2-6.3.

In a specific preferred embodiment, the stable liquid ophthalmic formulation comprises about 50 mg/ml of the VEGF antagonist (SEQ ID NO:4), 10 mM sodium phosphate buffer, 50 mM sodium chloride, 3% PEG, and 5% sucrose, pH about 6.2-6.3.

In a specific preferred embodiment, the stable liquid ophthalmic formulation comprises about 40 mg/ml of the VEGF antagonist (SEQ ID NO:4), 10 mM sodium phosphate buffer, 40 mM sodium chloride, 0.03% polysorbate, and 5% sucrose, pH about 6.2-6.3.

In a specific preferred embodiment, the stable liquid ophthalmic formulation comprises about 40 mg/ml of the VEGF antagonist (SEQ ID NO:4), 10 mM sodium phosphate buffer, 135 mM sodium chloride, and 0.03% polysorbate, pH about 6.2-6.3.

In another aspect, a stable liquid ophthalmic formulation is provided that comprises 1-100 mg/ml VEGF-specific fusion protein antagonist; 0.01-5% of one or more organic co-solvent(s); 5-40 mM of a buffering agent; and optionally 30-150 mM of one or more tonicity agent(s) and/or 1.0-7.5% of a stabilizing agent; having a pH between about 5.8-7.0.

In various embodiments, the VEGF antagonist (SEQ ID NO:4) is present at a concentration of about 10 to about 80 mg/ml. In various embodiments, the VEGF antagonist (SEQ ID NO:4) is present at a concentration of about 10, about 20, about 30, about 40, about 50, about 60, about 70, or about 80 mg/ml. In a preferred embodiment, the VEGF antagonist (SEQ ID NO:4) is present at a concentration of about 40 mg/ml.

In another embodiment, the stabilizing agent is selected from one or more of sucrose, sorbitol, glycerol, trehalose, and mannitol.

In another embodiment, the organic co-solvent is selected from one or more of polysorbate, for example, polysorbate 20 or polysorbate 80, polyethylene glycol (PEG), for example, PEG 3350, and propylene glycol.

In another embodiment, the buffer is a phosphate buffer, for example, sodium phosphate.

In another embodiment, the tonicity agent is a salt, for example, sodium chloride.

In one embodiment, the stable liquid ophthalmic formulation comprises 10 mM sodium phosphate buffer, about 0.03 to about 0.1% polysorbate and/or about 3% PEG or propylene glycol, about 40 mM sodium chloride, and about 5% sucrose. In a specific embodiment, the stable liquid ophthalmic formulation comprises 10 mM sodium phosphate buffer, about 0.03% polysorbate, about 40 mM sodium chloride, and about 5% sucrose. In another specific embodiment, the pH of the formulation is about 6.2 to about 6.3. In another specific embodiment, the pH is achieved by mixing mono- and dibasic sodium phosphate to the desired pH without acid/base titration.

In a specific embodiment, the stable liquid ophthalmic formulation consists essentially of a VEGF antagonist (SEQ ID NO:4) at 40 mg/ml, 10 mM sodium phosphate buffer, polysorbate at 0.03%, sodium chloride at 40 mM, and sucrose at 5%, pH 6.2-6.3.

In another aspect, a stable liquid ophthalmic formulation is provided that comprises about 10 to about 80 mg/ml VEGF antagonist, about 10 mM sodium phosphate buffer, about 0.03% polysorbate, and about 135 mM sodium chloride, pH 6.2 to 6.3.

In various embodiments, the VEGF antagonist (SEQ ID NO:4) is present at a concentration of about 10 to about 80 mg/ml. In various embodiments, the VEGF antagonist (SEQ ID NO:4) is present at a concentration of about 10, about 20, about 30, about 40, about 50, about 60, about 70, or about 80 mg/ml. In a specific embodiment, the VEGF antagonist (SEQ ID NO:4) is present at a concentration of about 40 mg/ml.

In one embodiment, the stable liquid ophthalmic formulation comprises 40 mg/ml of VEGF antagonist (SEQ ID NO:4), 10 mM sodium phosphate buffer, 0.03% polysorbate, and 135 mM sodium chloride at pH 6.2-6.3. In a specific embodiment, the stable liquid ophthalmic formulation consists essentially of 40 mg/ml of VEGF antagonist (SEQ ID NO:4), 10 mM sodium phosphate buffer, 0.03% polysorbate, and 135 mM sodium chloride at pH 6.2-6.3.

In another aspect, a lyophilizable formulation of a VEGF antagonist is provided, wherein upon lyophilization followed by reconstitution, a stable liquid ophthalmic formulation as described herein is obtained.

In another aspect, a lyophilizable formulation of a vascular endothelial growth factor (VEGF)-specific fusion protein antagonist is provided, comprising 5-50 mg/ml of the VEGF antagonist, 5-25 mM buffer, such as phosphate buffer, 0.01 to 0.15% of one or more of an organic co-solvent, such as polysorbate, propylene glycol and/or PEG, and optionally 1-10% of a stabilizing agent such as sucrose, sorbitol, trehalose, glycerol, or mannitol, pH about 5.8-7.0. In various embodiments, the VEGF antagonist (SEQ ID NO:4) is present at about 5, about 10, about 20, about 30, or about 40 mg/ml. In a specific embodiment, the lyophilizable ophthalmic formulation of the invention comprises 20 mg/ml of the VEGF antagonist, 10 mM sodium phosphate buffer, 0.03% polysorbate, 0.1% PEG, and 2.5% sucrose, pH about 6.2-6.3. In further embodiments, the lyophilizable formulation further comprises sodium chloride. In a specific embodiment, the sodium chloride is present at a concentration of about 20 mM. In another specific embodiment, the sodium chloride is present at a concentration of about 67.5 mM.

In another specific embodiment, the lyophilizable ophthalmic formulation of the invention comprises 20 mg/ml of the VEGF antagonist, 5 mM sodium phosphate buffer, 0.015% polysorbate, 20 mM sodium chloride, and 2.5% sucrose, pH about 6.2-6.3.

In another embodiment, the lyophilizable ophthalmic formulation comprises 5 mg/ml, 10 mg/ml, or 40 mg/ml VEGF antagonist, 5 mM sodium phosphate buffer, 0.015% polysorbate, 20 mM sodium chloride, and 2.5% sucrose, at pH 6.2-6.3. In a specific embodiment, the lyophilizable ophthalmic formulation consists essentially of 5 mg/ml, 10 mg/ml, or 40 mg/ml VEGF antagonist (SEQ ID NO:4), 5 mM sodium phosphate buffer, 0.015% polysorbate, 20 mM sodium chloride, and 2.5% sucrose, at pH 6.2-6.3.

In another specific embodiment, the lyophilizable ophthalmic formulation comprises 20 mg/ml of the VEGF antagonist, 5 mM sodium phosphate buffer, 0.015% polysorbate, and 67.5 mM sodium chloride, pH about 6.2-6.3. In a more specific embodiment, the lyophilizable ophthalmic formulation consists essentially of 20 mg/ml of the VEGF antagonist (SEQ ID NO:4), 5 mM sodium phosphate buffer, 0.015% polysorbate, and 67.5 mM sodium chloride, pH 6.2-6.3.

In another specific embodiment, the lyophilizable ophthalmic formulation comprises 5 mg/ml, 10 mg/ml, or 40 mg/ml VEGF antagonist, 5 mM sodium phosphate buffer, 0.015% polysorbate, and 67.5 mM sodium chloride, pH about 6.2-6.3. In a more specific embodiment, the lyophilizable ophthalmic formulation consists essentially of 5 mg/ml, 10 mg/ml, or 40 mg/ml VEGF antagonist (SEQ ID NO:4), 5 mM sodium phosphate buffer, 0.015% polysorbate, and 67.5 mM sodium chloride, pH about 6.2-6.3.

Generally, the reconstituted formulation is about 2 times the concentration of the pre-lyophilized formulation, e.g., a 20 mg fusion protein/ml pre-lyophilized formulation is reconstituted to a final formulation of 40 mg fusion protein/ml.

Generally, the lyophilized formulation is reconstituted with sterile water suitable for injection. In one embodiment, the reconstitution liquid is bacteriostatic water.

In another aspect, the invention features a method of producing a lyophilized formulation of a VEGF-specific fusion protein antagonist, comprising subjecting the lyophilizable formulation of the invention to lyophilization to generate a lyophilized formulation. The lyophilized formulation may be lyophilized by any method known in the art for lyophilizing a liquid.

In another related aspect, the invention features a method of producing a reconstituted lyophilized formulation of a VEGF antagonist, comprising reconstituting the lyophilized formulation of the invention to a reconstituted formulation. In one embodiment, the reconstituted formulation is twice the concentration of the pre-lyophilized formulation, e.g., the method of the invention comprises: (a) producing a pre-lyophilized formulation of a VEGF-specific fusion protein antagonist, (b) subjecting the pre-lyophilized formulation of step (a) to lyophilization; and (c) reconstituting the lyophilized formulation of step (b).

The invention further features ophthalmic formulations provided in a pre-filled syringe or vial, particularly suitable for intravitreal administration.

Other objects and advantages will become apparent from a review of the ensuing detailed description.

DETAILED DESCRIPTION OF THE INVENTION

The present invention is not limited to particular methods, and experimental conditions described, as such methods and conditions may vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to be limiting unless indicated, since the scope of the present invention will be limited only by the appended claims.

Unless stated otherwise, all technical and scientific terms and phrases used herein have the same meaning as commonly understood by one of ordinary skill in the art to which the invention belongs. Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, the preferred methods and materials are now described. All publications mentioned herein are incorporated herein by reference.

General Description

Safe handling and administration of formulations comprising proteins represent significant challenges to pharmaceutical formulators. Proteins possess unique chemical and physical properties that present stability problems: a variety of degradation pathways exist for proteins, implicating both chemical and physical instability. Chemical instability includes deamination, aggregation, clipping of the peptide backbone, and oxidation of methionine residues. Physical instability encompasses many phenomena, including, for example, aggregation and/or precipitation.

Chemical and physical stability can be promoted by removing water from the protein. Lyophilization (freeze-drying under controlled conditions) is commonly used for long-term storage of proteins. The lyophilized protein is substantially resistant to degradation, aggregation, oxidation, and other degenerative processes while in the freeze-dried state. The lyophilized protein may be reconstituted with water optionally containing a bacteriostatic preservative (e.g., benzyl alcohol) prior to administration.

Definitions

The term "carrier" includes a diluent, adjuvant, excipient, or vehicle with which a composition is administered. Carriers can include sterile liquids, such as, for example, water and oils, including oils of petroleum, animal, vegetable or synthetic origin, such as, for example, peanut oil, soybean oil, mineral oil, sesame oil and the like.

The term "excipient" includes a non-therapeutic agent added to a pharmaceutical composition to provide a desired consistency or stabilizing effect. Suitable pharmaceutical excipients include, for example, starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like.

The term "lyophilized" or "freeze-dried" includes a state of a substance that has been subjected to a drying procedure such as lyophilization, where at least 90% of moisture has been removed.

VEGF Antagonists

A VEGF antagonist is a compound capable of blocking or inhibiting the biological action of vascular endothelial growth factor (VEGF), and includes fusion proteins capable of trapping VEGF. In a preferred embodiment, the VEGF antagonist is the fusion protein of SEQ ID NO:2 or 4; more preferably, SEQ ID NO:4. In specific embodiments, the VEGF antagonist is expressed in a mammalian cell line such as a CHO cell and may be modified post-translationally. In a specific embodiment, the fusion protein comprises amino acids 27-457 of SEQ ID NO:4 and is glycosylated at Asn residues 62, 94, 149, 222 and 308. Preferably, the VEGF antagonist is a dimer composed of two fusion proteins of SEQ ID NO:4.

The VEGF antagonist of the methods and formulations of the invention can be prepared by any suitable method known in the art, or that comes to be known. The VEGF antagonist is preferably substantially free of protein contaminants at the time it is used to prepare the pharmaceutically acceptable formulation. By "substantially free of protein contaminants" is meant, preferably, that at least 90% of the weight of protein of the VEGF-specific fusion protein antagonist preparation used for making a formulation is VEGF fusion protein antagonist protein, more preferably at least 95%, most preferably at least 99%. The fusion protein is preferably substantially free of aggregates. "Substantially free of aggregates" means that at least 90% of the weight of fusion protein is not present in an aggregate at the time the fusion protein is used to prepare the pharmaceutically effective formulation. Unless stated otherwise, the phosphates employed are sodium phosphates and a desired buffering pH is achieved by mixing appropriate amounts of mono- and dibasic sodium phosphate.

Stable Liquid Ophthalmic Formulations

In one aspect, the invention provides a stable pharmaceutically acceptable formulation comprising a VEGF antagonist, wherein the formulation is a liquid formulation suitable for ophthalmic use. Preferably, the liquid formulation comprises a pharmaceutically effective amount of the VEGF antagonist. The formulation can also comprise one or more

pharmaceutically acceptable carriers, buffers, tonicity agents, stabilizers, and/or excipients. An example of a pharmaceutically acceptable liquid formulation comprises a VEGF antagonist in a pharmaceutically effective amount, a buffer, an organic co-solvent such as polysorbate, a tonicity agent such as NaCl, and optionally, a stabilizer such as sucrose or trehalose.

Stability is determined in a number of ways at specified time points, including determination of pH, visual inspection of color and appearance, determination of total protein content by methods known in the art, e.g., UV spectroscopy, and purity is determined by, for example, SDS-PAGE, size-exclusion HPLC, bioassay determination of activity, isoelectric focusing, and isoaspartate quantification. In one example of a bioassay useful for determining VEGF antagonist activity, a BAF/3 VEGFR1/EPOR cell line is used to determine VEGF165 binding by the VEGF antagonist of the invention.

Liquid formulations can be stored in an oxygen-deprived environment. Oxygen-deprived environments can be generated by storing the formulations under an inert gas such as, for example, nitrogen or argon. Liquid formulations are preferably stored at about 5° C.

Ophthalmic Lyophilized Formulations

In one aspect of the invention, an ophthalmically acceptable formulation comprising a VEGF antagonist is provided, wherein the formulation is a lyophilizable formulation. Lyophilizable formulations can be reconstituted into solutions, suspensions, emulsions, or any other suitable form for administration or use. Lyophilizable formulations are typically first prepared as liquids, then frozen and lyophilized. The total liquid volume before lyophilization can be less, equal to, or more than, the final reconstituted volume of the lyophilized formulation. The lyophilization process is well known to those of ordinary skill in the art, and typically includes sublimation of water from a frozen formulation under controlled conditions.

Lyophilized formulations can be stored at a wide range of temperatures. Lyophilized formulations may be stored below 25° C., for example, refrigerated at 2-8° C., or at room temperature (e.g., approximately 25° C.). Preferably, lyophilized formulations are stored below about 25° C., more preferably, at about 4-20° C.; below about 4° C.; below about −20° C.; about −40° C.; about −70° C., or about −80° C. Stability of the lyophilized formulation may be determined in a number of ways known to the art, for example, by visual appearance of the cake and/or by moisture content.

Lyophilized formulations are typically reconstituted for use by addition of an aqueous solution to dissolve the lyophilized formulation. A wide variety of aqueous solutions can be used to reconstitute a lyophilized formulation. Preferably, lyophilized formulations are reconstituted using water. Lyophilized formulations are preferably reconstituted with a solution consisting essentially of water (e.g., USP WFI, or water for injection) or bacteriostatic water (e.g., USP WFI with 0.9% benzyl alcohol). However, solutions comprising buffers and/or excipients and/or one or more pharmaceutically acceptable carries can also be used.

Freeze-dried or lyophilized formulations are typically prepared from liquids, that is, from solutions, suspensions, emulsions, and the like. Thus, the liquid that is to undergo freeze-drying or lyophilization preferably comprises all components desired in a final reconstituted liquid formulation. As a result, when reconstituted, the freeze-dried or lyophilized formulation will render a desired liquid formulation upon reconstitution.

EXAMPLES

Before the present methods are described, it is to be understood that this invention is not limited to particular methods, and experimental conditions described, as such methods and conditions may vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to be limiting, since the scope of the present invention will be limited only to the appended claims.

As used in this specification and the appended claims, the singular forms “a”, “an”, and “the” include plural references unless the context clearly dictates otherwise. Thus for example, a reference to “a method” includes one or more methods, and/or steps of the type described herein and/or which will become apparent to those persons skilled in the art upon reading this disclosure and so forth.

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, the preferred methods and materials are now described. All publications mentioned herein are incorporated herein by reference in their entirety.

Example 1. Stability of 50 mg/ml VEGF Trap Liquid Formulation Stored at 5° C. in 3 ml Glass Vials

An ophthalmic liquid formulation containing 50 mg/ml VEGF Trap (SEQ ID NO:4), 10 mM phosphate, 50 mM NaCl, 0.1% polysorbate 20, 5% sucrose, and pH 6.25, was stored at 5° C. in 3 ml glass vials and samples tested at 3, 6, 9, 12, 18 and 24 months. Stability was determined by SE-HPLC The results are shown in Table 1. Turbidity was measured at OD_{405} nm; and percent recovered protein and purity by size exclusion HPLC.

TABLE 1

Stability of 50 mg/ml VEGF Trap Protein (VGFT-SS065)

Months	Visual Appearance	Turbidity (OD_{405} nm)	pH	% VEGF Trap Recovered	% VEGF Trap Native Configuration
0	Pass	0.00	6.2	100	98.8
3	Pass	0.00	6.2	101	98.7
6	Pass	0.01	6.3	100	98.3
9	Pass	0.01	6.3	101	98.3
12	Pass	0.01	6.3	104	98.4
18	Pass	0.01	6.3	96	98.1
24	Pass	0.01	6.3	105	98.1

Example 2. Stability of 50 mg/ml VEGF Trap Liquid Formulation Stored at 5° C. in 3 ml Glass Vials

A liquid formulation containing 50 mg/ml VEGF Trap (SEQ ID NO:4), 10 mM phosphate, 50 mM NaC1, 3% polyethylene glycol 3350, 5% sucrose, and pH 6.25, was stored at 5° C. in 3 nil glass vials and samples tested at 3, 6,

9, 12, 18 and 24 months. Stability results are shown in Table 2. Turbidity, percent recovered protein and purity was determined as described above.

TABLE 2

Stability of 50 mg/ml VEGF Trap Protein (VGFT-SS065)

Months	Visual Appearance	Turbidity	pH	% VEGF Trap Recovered	% VEGF Trap Native Configuration
0	Pass	0.00	6.2	100	98.9
3	Pass	0.00	6.1	104	98.5
6	Pass	0.01	6.3	99	98.3
9	Pass	0.00	6.3	102	97.6
12	Pass	0.01	6.3	103	98.0
18	Pass	0.00	6.3	113	97.7
24	Pass	0.00	6.2	106	97.6

Example 3. Stability of 40 mg/ml VEGF Trap Liquid Formulation Stored at 5° C. in 3 ml Glass Vials

A liquid formulation containing 40 mg/ml VEGF Trap (SEQ ID NO:4), 10 mM phosphate, 40 mM NaCl, 0.03% polysorbate 20, 5% sucrose, and pH 6.3, was stored at 5° C. in 3 ml glass vials and samples tested at 0.5, 1, 2, 3, and 4 months. Stability results are shown in Table 3. Turbidity, percent recovered protein and purity was determined as described above.

TABLE 3

Stability of 40 mg/ml VEGF Trap Protein (VGFT-SS207)

Months	Visual Appearance	Turbidity	pH	% VEGF Trap Recovered	% VEGF Trap Native Configuration
0	Pass	0.00	6.3	100	99.5
0.5	Pass	0.00	6.3	99	99.4
1	Pass	0.00	6.2	98	99.5
2	Pass	0.00	6.2	95	99.2
3	Pass	0.01	6.4		
4	Pass	0.01	6.3		

Example 4. Stability of 40 mg/ml VEGF Trap Liquid Formulation Stored at 5° C. in Pre-Filled Glass Syringe

A liquid formulation containing 40 mg/ml VEGF trap (SEQ ID NO:4), 10 mM phosphate, 40 mM NaCl, 0.03% polysorbate 20, 5% sucrose, and pH 6.3, was stored at 5° C. in 1 ml prefilled luer glass syringe with 4023/50 FluroTec coated plunger and samples tested at 0.5, 1, 2, 3, and 4 months. Stability results are shown in Table 4. Turbidity, percent recovered protein and purity was determined as described above.

TABLE 4

Stability of 40 mg/ml VEGF Trap Protein (VGFT-SS207)

Months	Visual Appearance	Turbidity	pH	% VEGF Trap Recovered	% VEGF Trap Native Configuration
0	Pass	0.00	6.3	100	99.4
0.5	Pass	0.00	6.3	100	99.3

TABLE 4-continued

Stability of 40 mg/ml VEGF Trap Protein (VGFT-SS207)

Months	Visual Appearance	Turbidity	pH	% VEGF Trap Recovered	% VEGF Trap Native Configuration
1	Pass	0.00	6.3	100	99.4
2	Pass	0.00	6.3	97	99.1
3	Pass	0.01	6.4		
4	Pass	0.01	6.3		

Example 5. Stability of 40 mg/ml VEGF Trap Liquid Formulation Stored at 5° C. in 3 ml Glass Vials

A liquid formulation containing 40 mg/ml VEGF trap (SEQ ID NO:4), 10 mM phosphate, 135 mM NaCl, 0.03% polysorbate 20, and pH 6.3, was stored at 5° C. in 3 ml glass vials and samples tested at 0.5, 1, 2, 3, and 4 months. Stability results are shown in Table 5. Turbidity, percent recovered protein and purity was determined as described above.

TABLE 5

Stability of 40 mg/ml VEGF Trap Protein (VGFT-SS203)

Months	Visual Appearance	Turbidity	pH	% VEGF Trap Recovered	% VEGF Trap Native Configuration
0	Pass	0.00	6.3	100	99.3
0.5	Pass	0.00	6.2	87	99.2
1	Pass	0.00	6.2	88	99.1
2	Pass	0.00	6.3	103	99.2
3	Pass	0.00	6.3	88	99.0
4	Pass	0.00	6.2	85	98.9
5	Pass	0.00	6.3	84	99.0

Example 6. Stability of 40 mg/ml VEGF Trap Liquid Formulation Stored at 5° C. in 1 ml Pre-Filled Glass Syringe

A liquid formulation containing 40 mg/ml VEGF trap (SEQ ID NO:4), 10 mM phosphate, 135 mM NaCl, 0.03% polysorbate 20, and pH 6.3, was stored at 5° C. in 1 ml prefilled glass luer syringe with 4023/50 FluroTec coated plunger and samples tested at 0.5, 1, 2, 3, 4, and 5 months. Stability results are shown in Table 6. Turbidity, percent recovered protein and purity was determined as described above.

TABLE 6

Stability of 40 mg/ml VEGF Trap Protein (VGFT-SS203)

Months	Visual Appearance	Turbidity	pH	% VEGF Trap Recovered	% VEGF Trap Native Configuration
0	Pass	0.00	6.3	100	99.2
0.5	Pass	0.01	6.3	101	99.2
1	Pass	0.00	6.3	101	99.2
2	Pass	0.00	6.3	—	—
3	Pass	0.01	6.3	102	99.1
4	Pass	0.01	6.3	103	98.8
5	Pass	0.00	6.3	99	98.9

Example 7. Stability of Lyophilized 20 mg/ml VEGF Trap Formulation Stored at 5° C. in 3 ml Glass Vials and Reconstituted to 40 mg/ml

0.8 ml of a liquid formulation containing 20 mg/ml VEGF trap (SEQ ID NO:4), 5 mM phosphate, 20 mM NaCl, 0.015% polysorbate 20, 2.5% sucrose, and pH 6.3, were lyophilized in 3 ml glass vials. Samples were stored at 5° C. and tested at 1, and 2 months. VEGF trap was reconstituted to a final concentration of 40 mg/ml VEGF Trap (final volume of 0.4 ml). Stability results are shown in Table 7 (t=time in months; *=visual appearance; **=reconstitution time). Turbidity, percent recovered protein and purity was determined as described above.

TABLE 7

Stability of Lyophilized 20 mg/ml VEGF Trap Protein (VGFT-SS216)

t	Vis. App.*	Recon. Time** (min)	Vis. App.* Reconst'd Liquid	Turbidity	pH	% VEGF Trap Recovered	% VEGF Trap Native Config.
0	Pass	0.6	Pass	0.00	6.3	100	99.5
1	Pass	0.6	Pass	0.01	6.3	106	99.4
2	Pass	0.4	Pass	0.01	6.2	103	99.3

Example 8. Stability of Lyophilized 20 mg/ml VEGF Trap Formulation Stored at 5° C. in 3 ml Glass Vials

0.8 ml of a liquid formulation containing 20 mg/ml VEGF trap (SEQ ID NO:4), 5 mM phosphate, 67.5 mM NaCl, 0.015% polysorbate 20, and pH 6.3, were lyophilized in 3 ml glass vials. Samples were stored at 5° C. and tested at 1, 2, and 3 months. VEGF trap was reconstituted to a final concentration of 40 mg/ml VEGF trap (final volume of 0.4 ml). Stability results are shown in Table 8 (t=time in months; *=visual appearance; **=reconstitution time).

TABLE 8

Stability of Lyophilized 20 mg/ml VEGF Trap Protein (VGFT-SS216)

t	Vis. App.*	Recon. Time** (min)	Vis. App. Reconst'd Liquid	Turbidity	pH	% VEGF Trap Recovered	% VEGF Trap Native Config.
0	Pass	0.7	Pass	0.00	6.3	100	99.0
1	Pass	0.7	Pass	0.01	6.2	105	98.9
2	Pass	0.4	Pass	0.01	6.2	103	98.9

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Leu Ser Pro Ser His Gly Ile Glu Leu Ser Val Gly Glu Lys Leu Val
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Leu Asn Cys Thr Ala Arg Thr Glu Leu Asn Val Gly Ile Asp Phe Asn
145                 150                 155                 160

Trp Glu Tyr Pro Ser Ser Lys His Gln His Lys Lys Leu Val Asn Arg
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Asp Leu Lys Thr Gln Ser Gly Ser Glu Met Lys Lys Phe Leu Ser Thr
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Leu Thr Ile Asp Gly Val Thr Arg Ser Asp Gln Gly Leu Tyr Thr Cys
        195                 200                 205

Ala Ala Ser Ser Gly Leu Met Thr Lys Lys Asn Ser Thr Phe Val Arg
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Val His Glu Lys Gly Pro Gly Asp Lys Thr His Thr Cys Pro Pro Cys
225                 230                 235                 240

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
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Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
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Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
        275                 280                 285
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Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
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His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
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Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
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Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
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Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
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Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
385                 390                 395                 400

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
                405                 410                 415

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
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cccgaaatta tacacatgac tgaaggaagg gagctcgtca ttccctgccg ggttacgtca    180

cctaacatca ctgttacttt aaaaaagttt ccacttgaca ctttgatccc tgatggaaaa    240

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gggcttctga cctgtgaagc aacagtcaat gggcatttgt ataagacaaa ctatctcaca    360

catcgacaaa ccaatacaat catagatgtg gttctgagtc cgtctcatgg aattgaacta    420

tctgttggag aaaagcttgt cttaaattgt acagcaagaa ctgaactaaa tgtggggatt    480

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ctaaaaaccc agtctgggag tgagatgaag aaatttttga gcaccttaac tatagatggt    600

gtaacccgga gtgaccaagg attgtacacc tgtgcagcat ccagtgggct gatgaccaag    660

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aagccgcggg aggagcagta caacagcacg taccgtgtgg tcagcgtcct caccgtcctg    960

caccaggact ggctgaatgg caaggagtac aagtgcaagg tctccaacaa agccctccca   1020

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aactacaaga ccacgcctcc cgtgctggac tccgacggct ccttcttcct ctacagcaag   1260

ctcaccgtgg acaagagcag gtggcagcag gggaacgtct tctcatgctc cgtgatgcat   1320

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Phe Val Glu Met Tyr Ser Glu Ile Pro Glu Ile Ile His Met Thr Glu
        35                  40                  45

Gly Arg Glu Leu Val Ile Pro Cys Arg Val Thr Ser Pro Asn Ile Thr
    50                  55                  60

Val Thr Leu Lys Lys Phe Pro Leu Asp Thr Leu Ile Pro Asp Gly Lys
65                  70                  75                  80

Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe Ile Ile Ser Asn Ala Thr
                85                  90                  95

Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu Ala Thr Val Asn Gly His
            100                 105                 110

Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg Gln Thr Asn Thr Ile Ile
        115                 120                 125

Asp Val Val Leu Ser Pro Ser His Gly Ile Glu Leu Ser Val Gly Glu
    130                 135                 140

Lys Leu Val Leu Asn Cys Thr Ala Arg Thr Glu Leu Asn Val Gly Ile
145                 150                 155                 160

Asp Phe Asn Trp Glu Tyr Pro Ser Ser Lys His Gln His Lys Lys Leu
                165                 170                 175

Val Asn Arg Asp Leu Lys Thr Gln Ser Gly Ser Glu Met Lys Lys Phe
            180                 185                 190

Leu Ser Thr Leu Thr Ile Asp Gly Val Thr Arg Ser Asp Gln Gly Leu
        195                 200                 205

Tyr Thr Cys Ala Ala Ser Ser Gly Leu Met Thr Lys Lys Asn Ser Thr
    210                 215                 220

Phe Val Arg Val His Glu Lys Asp Lys Thr His Thr Cys Pro Pro Cys
225                 230                 235                 240

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
                245                 250                 255

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
            260                 265                 270

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
        275                 280                 285

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
    290                 295                 300

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
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-continued

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305                 310                 315                 320

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
                325                 330                 335

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
            340                 345                 350

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
        355                 360                 365

Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
    370                 375                 380

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
385                 390                 395                 400

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
                405                 410                 415

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
            420                 425                 430

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
        435                 440                 445

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
    450                 455
```

We claim:

1. A vial comprising an ophthalmic formulation suitable for intravitreal administration that comprises:

a vascular endothelial growth factor (VEGF) antagonist

an organic co-solvent,

a buffer, and

a stabilizing agent,

wherein said VEGF antagonist fusion protein is glycosylated and comprises amino acids 27-457 of SEQ ID NO:4; and

wherein at least 98% of the VEGF antagonist is present in native conformation following storage at 5° C. for two months as measured by size exclusion chromatography.

2. The vial of claim **1**, wherein the concentration of said VEGF antagonist fusion protein is 40 mg/ml, and wherein said organic co-solvent comprises polysorbate.

3. The vial of claim **2**, wherein said organic co-solvent comprises 0.01% to 3% polysorbate.

4. The vial of claim **2**, wherein said organic co-solvent comprises about 0.03% to about 0.1% polysorbate 20.

5. The vial of claim **2**, wherein said organic co-solvent comprises 0.01% to 3% polysorbate 20.

6. The vial of claim **5**, wherein said buffer comprises a phosphate buffer.

7. The vial of claim **5**, wherein said buffer comprises 5-25 mM buffer.

8. The vial of claim **5**, wherein said buffer comprises a pH between about 5.8-7.0.

9. The vial of claim **5**, wherein said buffer comprises a pH about 6.2-6.3.

10. The vial of claim **5**, wherein said stabilizing agent comprises a sugar.

11. The vial of claim **10**, wherein said sugar is selected from the group consisting of sucrose, sorbitol, glycerol, trehalose, and mannitol.

12. The vial of claim **5**, wherein said stabilizing agent comprises 1.0-7.5% of sucrose.

13. The vial of claim **5**, wherein said formulation further comprises a tonicity agent.

14. The vial of claim **5**, wherein said VEGF antagonist fusion protein is glycosylated at asparagine residues corresponding to asparagine residues 62, 94, 149, 222 and 308 of SEQ ID NO: 4.

15. The vial of claim **5**, wherein said formulation is capable of providing a turbidity of 0.01 or lower at OD_{405} after 2 month storage at 5° C.

16. The vial of claim **5**, wherein at least 99% of said VEGF antagonist fusion protein is present in native conformation after 2 month storage at 5° C. as measured by size exclusion chromatography.

17. The vial of claim **5**, wherein at least 98% of said VEGF antagonist fusion protein is present in native conformation following storage at 5° C. for 24 months as measured by size exclusion chromatography.

18. The vial of claim **5**, wherein said formulation does not contain phosphate.

19. The vial of claim **5**, wherein said formulation does not contain trehalose.

20. The vial of claim **5**, wherein said stabilizing agent comprises 1.0-10% of sucrose.

21. The vial of claim **20**, wherein said formulation further comprises a tonicity agent.

22. The vial of claim **20**, wherein said VEGF antagonist fusion protein is glycosylated at asparagine residues corresponding to asparagine residues 62, 94, 149, 222 and 308 of SEQ ID NO: 4.

23. The vial of claim **20**, wherein said formulation is capable of providing a turbidity of 0.01 or lower at OD_{405} after 2 month storage at 5° C.

24. The vial of claim **20**, wherein at least 99% of said VEGF antagonist fusion protein is present in native conformation after 2 month storage at 5° C. as measured by size exclusion chromatography.

25. The vial of claim **20**, wherein at least 98% of said VEGF antagonist fusion protein is present in native conformation following storage at 5° C. for 24 months as measured by size exclusion chromatography.

26. A pre-filled syringe comprising an ophthalmic formulation suitable for intravitreal administration comprising:

a vascular endothelial growth factor (VEGF) antagonist fusion protein,

an organic co-solvent,

a buffer, and

a stabilizing agent;

wherein said VEGF antagonist fusion protein is glycosylated and comprises amino acids 27-457 of SEQ ID NO:4; and

wherein at least 98% of said VEGF antagonist fusion protein is present in native conformation following storage at 5° C. for two months as measured by size exclusion chromatography.

27. The pre-filled syringe of claim **26**, wherein the concentration of said VEGF antagonist fusion protein is 40 mg/ml, and wherein said organic co-solvent comprises polysorbate.

28. The pre-filled syringe of claim **27**, wherein said organic co-solvent comprises 0.01% to 3% polysorbate.

29. The pre-filled syringe of claim **27**, wherein said organic co-solvent comprises about 0.03% to about 0.1% polysorbate 20.

30. The pre-filled syringe of claim **27**, wherein said organic co-solvent comprises 0.01% to 3% polysorbate 20.

31. The pre-filled syringe of claim **30**, wherein said buffer comprises a phosphate buffer.

32. The pre-filled syringe of claim **30**, wherein said buffer comprises 5-25 mM buffer.

33. The pre-filled syringe of claim **30**, wherein said buffer comprises a pH between about 5.8-7.0.

34. The pre-filled syringe of claim **30**, wherein said buffer comprises a pH about 6.2-6.3.

35. The pre-filled syringe of claim **30**, wherein said stabilizing agent comprises a sugar.

36. The pre-filled syringe of claim **35**, wherein said sugar is selected from the group consisting of sucrose, sorbitol, glycerol, trehalose, and mannitol.

37. The pre-filled syringe of claim **30**, wherein said stabilizing agent comprises 1.0-7.5% of sucrose.

38. The pre-filled syringe of claim **30**, wherein said formulation further comprises a tonicity agent.

39. The pre-filled syringe of claim **30**, wherein said VEGF antagonist fusion protein is glycosylated at asparagine residues corresponding to asparagine residues 62, 94, 149, 222 and 308 of SEQ ID NO: 4.

40. The pre-filled syringe of claim **30**, wherein said formulation is capable of providing a turbidity of 0.01 or lower at OD_{405} after 2 month storage at 5° C.

41. The pre-filled syringe of claim **30**, wherein at least 99% of said VEGF antagonist fusion protein is present in native conformation after 2 month storage at 5° C. as measured by size exclusion chromatography.

42. The pre-filled syringe of claim **30**, wherein at least 98% of said VEGF antagonist fusion protein is present in native conformation following storage at 5° C. for 24 months as measured by size exclusion chromatography.

43. The pre-filled syringe of claim **30**, wherein said formulation does not contain phosphate.

44. The pre-filled syringe of claim **30**, wherein said formulation does not contain trehalose.

45. The pre-filled syringe of claim **30**, wherein said stabilizing agent comprises 1.0-10% of sucrose.

46. The pre-filled syringe of claim **45**, wherein said formulation further comprises a tonicity agent.

47. The pre-filled syringe of claim **45**, wherein said VEGF antagonist fusion protein is glycosylated at asparagine residues corresponding to asparagine residues 62, 94, 149, 222 and 308 of SEQ ID NO: 4.

48. The pre-filled syringe of claim **45**, wherein said formulation is capable of providing a turbidity of 0.01 or lower at OD_{405} after 2 month storage at 5° C.

49. The pre-filled syringe of claim **45**, wherein at least 99% of said VEGF antagonist fusion protein is present in native conformation after 2 month storage at 5° C. as measured by size exclusion chromatography.

50. The pre-filled syringe of claim **45**, wherein at least 98% of said VEGF antagonist fusion protein is present in native conformation following storage at 5° C. for 24 months as measured by size exclusion chromatography.

51. An ophthalmic formulation comprising:

(a) 40 mg/ml of a glycosylated VEGF antagonist fusion protein comprising amino acids 27-457 of SEQ ID NO:4;

(b) 0.03% to 0.1% polysorbate;

(c) 5-40 mM of sodium phosphate buffer, pH between 5.8-7.0; and

(d) sucrose;

wherein the ophthalmic formulation is suitable for intravitreal administration; and

wherein at least 98% of the VEGF antagonist is present in native conformation following storage at 5° C. for 2 months as measured by size exclusion chromatography.

52. The formulation of claim **51**, wherein said formulation comprises at least 5% sucrose.

53. The formulation of claim **51**, wherein said formulation comprises 1-10% sucrose.

54. A pre-filled syringe suitable for intravitreal administration comprising the formulation of claim **51**.

55. A vial suitable for intravitreal administration comprising the formulation of claim **51**.

56. The formulation of claim **51**, wherein said formulation comprises 10 mM sodium phosphate buffer, 0.03% polysorbate, 5% sucrose, and a pH between 6.2-6.3.

57. A pre-filled syringe suitable for intravitreal administration comprising the formulation of claim **56**.

58. A vial suitable for intravitreal administration comprising the formulation of claim **56**.

59. The formulation of claim **56**, wherein said formulation further comprises 40 mM NaCl.

60. A pre-filled syringe suitable for intravitreal administration comprising the formulation of claim **59**.

61. A vial suitable for intravitreal administration comprising the formulation of claim **59**.

62. The formulation of claim **59**, wherein said VEGF antagonist fusion protein is glycosylated at asparagine residues corresponding to asparagine residues 62, 94, 149, 222 and 308 of SEQ ID NO: 4.

63. A pre-filled syringe suitable for intravitreal administration comprising the formulation of claim **62**.

64. A vial suitable for intravitreal administration comprising the formulation of claim **62**.

* * * * *

Graham Ex. 2

Protocol For Stability Study #VGFT-SS207

Purpose:

Determine the stability of 40 mg/mL VEGF Trap in the Polysorbate 20 based intravitreal formulation when packaged in a pre-filled syringe with six different component combinations. The stability of VEGF trap when filled in glass vials will serve as the control in this study.

Test Article:

The basic composition of the formulation (lot # C2-5688-103-SPS) is:

10 mM Phosphate
40 mM NaCl
0.03% PS20
5 % Sucrose
40 mg/mL VEGF Trap
pH 6.25

Preparation:

The Formulation and Fill Group at Regeneron Pharmaceuticals, Inc., Rensselaer, NY prepared 750 mLs of formulation. The formulation was shipped in a 1 liter polycarbonate bottle to Vetter in Germany where pre-filled syringes (150 µL/syringe) were manufactured according to Protocol VDS-HF-051033 and Table 1 below. The remaining solution and filled syringes were shipped back to the formulation Development Group at Regeneron Pharmaceuticals, Inc., Tarrtown, NY. The FDG will fill ~~fourtytwo~~ thirty nine JC 1/17/06 (39) ~~(42)~~ 2 mL glass vials with 0.5 mL of formulation from the remaining solution to be used as controls. An additional ~~five (5)~~ two (2) JC 1/17/06 2 mL glass vials will be filled with 1.0 mL of formulation for use in syringeability studies. All vials used in this study are cleaned and JC 1/17/06. depyrogenated prior to filling. This study will use 146 syringes of each component combination. Table 1 contains a description of each component combination used in this study. These combinations will be referred to as device 1, device 2, etc. in the text of this protocol.

JC 1/17/06

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Table 1.

Device #	Glass barrel	Siliconization	Plunger	Closure Part
# 1	1 ml-l luer cone (OVS 10.6)	1000 cSt. silicone oil, spray siliconization	HV FM457 (V01311 or V00951)	HV FM27
# 2	1 ml-l luer cone (OVS 10.6)	1000 cSt. silicone oil, spray siliconization	West 4432/50 (V00916)	West 4023/50
# 3	1 ml-l luer cone (OVS 10.6)	1000 cSt. silicone oil, spray siliconization	West 4023/50, fluorotech (V00633)	West 4023/50
# 4	1ml-l staked needle **27 G**	1000 cSt. silicone oil, spray siliconization	West 4432/50 (V00916)	RNS FM27
# 5	1ml-l staked needle **27 G**	1000 cSt. silicone oil, spray siliconization	West 4023/50, fluorotech (V00633)	RNS FM27
# 6	1 ml-l luer cone (OVS 10.6)	Silicone emulsion, spray siliconization + heat tunnel	HV FM457 (V01311 or V00951)	HV FM27
# 7	2 mL glass vials	Not applicable	Not applicable	West Grey butyl rubber stopper 1888

Storage Conditions:

Storage conditions and sampling intervals for each device are listed in Table 2 below. At each storage condition and time point one (1) 2mL glass vial will be removed. Three syringes will be pulled at each time point for each device with the storage conditions in a needle up orientation. One syringe will be pulled at each time point for each device with the storage conditions in a needle down orientation.

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Table 2.

Storage condition	Total no. of syringes/ vials stored	Sampling intervals	No. of Syringes /vials pulled
Long-term			
–40°C (needle up)	16/8	TBD	TBD
+5°C (needle up)	48/15	0.5, 1, 2, 3[b], 4, 5, 6, 9, 12[b], 15, 18, and 24[b] (months), x[a], x[a], x[a]	3/1
+5°C (needle down)	15/0	0.5, 1, 2, 3, 4, 5, 6, 9, 12, 15, 18, and 24 (months), x[a], x[a], x[a]	1/0
Stress			
+25°C (needle up)	24/8	0.5, 1, 2, 3, 4, 5, and 6 (months), x[a]	3/1
+25°C (needle down)	9/0	0.5, 1, 2, 3, 4, 5, and 6 (months)), x[a], x[a]	1/0
+37°C (needle up)	16/5	7, 14, 21, and 28[b] (days), x[a]	3/1
+37°C (needle down)	6/0	7, 14, 21, and 28 (days)), x[a], x[a]	1/0
t=0			
5°C / -80°C	12/3	0 (days), x[a], x[a]	4[c]/1

[a] Syringes and vials will be stored under the noted storage condition and pulled whenever it is deemed necessary.
[b] An additional syringe will be pulled at those time points where the binding assay will be performed (37°C 28 days, 5°C 3, 12, and 24 months).
[C] t=0 for all temperatures greater than 5°C is defined as the time when the syringes are placed into the incubator. For the 5°C syringes t=0 is defined as the day the visual inspection is perfomed. 4 t=0 syringes of each device will be stored at 5°C until analysis is initiated on replicates 1- 4, (no more than 5 days following the initiation of the protocol). At this time the remaining t=0 syringes will each be gently ejected into ~~a~~ separate depyrogenated 2 mL glass vials within a laminar flow hood and then stored at -80°C for future use. JC 1/17/06

Syringe Stress Testing:

A syringeability stress test will be performed on this formulation in an attempt to differentiate the VEGF Trap stability in different formulations (VGFT-SS200 – VGFT-SS208). The test will be performed at the beginning of the study on vials filled with the remainder of formulation sent back from Vetter. Two levels of syringe stress will be evaluated, 1X Syringeability and 4X Syringeability. The procedure for each stress level is described below.

1X Syringeability

1.0 mL of air will be loaded into a 1cc (1mL) BD slip tip syringes (catalogue #309602) with a 27 gauge ½ inch needle attached. The 1.0 mL of air will be dispensed into the

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upright vial so as not to eject it into the solution. The vial will be inverted and withdrawable contents of the vial will then be loaded into the syringe. The filled syringe and 27 gauge ½ inch needle will be incubated at 25°C for 1 hour. Upon completion of incubation the 27 gauge ½ inch needle will be removed and replaced with a 30 gauge ½ inch needle. The contents of the syringe will be gently ejected into a fresh stoppered 2ml glass vial. The formulation will be analyzed as described below.

4X Syringeability
1.0 mL of air will be loaded into a 1cc (1mL) BD slip tip syringe (catalogue #309602) with a 27 gauge ½ inch needle attached. The 1.0 mL of air will be dispensed into the upright vial so not to eject it into the solution. The vial will be inverted and withdrawable content of the vial will then be loaded into the syringe. Maintaining the vial in an inverted position the contents of the syringe will be gently injected back into the vial. The loading and injection cycle will be repeated 2 additional times. After loading the syringe the fourth time the filled syringe and 27 gauge ½ inch needle will be incubated at 25°C for 1 hour. Upon completion of incubation the 27 gauge ½ inch needle will be removed and replaced with a 30 gauge ½ inch needle. The syringe will be gently ejected into a fresh stoppered 2ml glass vial. The formulation will be analyzed as described below.

Analyses to Be Performed:

Four pre-filled syringes will be removed from 5°C, 25°C and 37°C incubators at every specified time point, with a fifth pre-filled syringe removed when a binding assay is scheduled. The syringes will be numbered as they are removed from the incubator as described in Table 3 below. Pre-filled syringes will only be removed for analysis from the -40°C chamber if instability is observed at 5°C. After 3 months of storage at – 40°C 4 of the syringes will be removed and examined for the ability of the syringes to withstand the freezing process.

Table 3.

Syringe number for syringes/time point	Orientation	Analysis
1	Needle up	In house
2	Needle up	In house
3	Needle up	In house
4	Needle down	In house
5*	Needle up	QC/ binding assay

*This syringe will only be pulled at designated time points when the binding assay will be performed (37°C 28 days and 5°C 3, 12, and 24 months).

Delivery via syringe:

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After devices 1, 2, 3 and 6 have undergone the visual inspection a 27 gauge ½ inch needle will be attached to the syringe and the sample will be ejected prior to the analysis described below.

After devices 4 and 5 have undergone the visual inspection the sample will be ejected through the attached 27 gauge needle prior to the analysis described below.

Table 4 provides a summary of assays performed on the pre-filled syringes for devices 1 through 6. At each time point all assays will be performed on device 7 – (the single control vial filled with 500 μL of formulation). If instability is observed at 5°C, at the discretion of the Study Director or the Director of Formulation Development syringes may be removed from storage at -40°C for analysis.

Table 4.

Assay	Volume required	Syringe #
Appearance/color in syringe or control vial	-	All syringes
Appearance/color ejected from a syringe into a vial	-	Syringe 3
OD @ 405 nm	100 μL	Syringe 1
pH	100 μL	Syringe 1
VEGF Trap Concentration	By SE-HPLC	Syringes 1 - 4 (3 needle up & 1 needle down)
SE-HPLC	5 μL/assay	Syringes 1 - 4 (3 needle up & 1 needle down)
RP-HPLC	5 μL/assay	Syringe 2
SDS-PAGE Reduced	5 μL/assay	Syringe 3
SDS-PAGE Non reduced	5 μL/assay	Syringe 3
Binding Assay	50 μL	Syringe 5
FTIR	10 μL	Syringe 1
Isoquant	30 μL	Syringe 3

Osmolality: The osmolality of the formulations after they are received by the Formulation Development Group, Tarrytown, NY, will be measured and recorded.

Visual Inspection: Every syringe and vial in this study, including the 1x and 4x syringeability samples, will be visually inspected for the presence of particulates. During this inspection the syringe or vial may be inverted as required to determine the presence of particulates. If particulates or precipitates are observed in the solution their presence will be recorded. If no particulates or precipitates are found, the result "clear, no ppt" will be recorded. Any other problems that are observed will be recorded. An additional

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visual inspection as described above will be performed on the contents of syringe 3 after they are ejected into a clean depyrogenated vial.

Optical Density (OD @ 405 nm): Optical density (OD 405 nm) will be performed on one of the three needle up pre-filled syringes (syringe 1) pulled at each time point and on the 1x and 4x syringeability samples. These measurements will be made using 100 μL of sample and the microplate reader. Optical density, at 405 nm, measures the turbidity and therefore can be indicative of the presence of precipitation.

pH: The pH of the formulation contained in one of the three needle up pre-filled syringes (syringe 1) pulled at each time point will be measured. After both pH and OD measurements, the sample will be returned to the vial and used for further analysis.

Concentration (Recovery): SE-HPLC analysis as described below will be performed to determine the amount of protein that is actually recovered from syringes #1-#4 and the vial at each time point, including the 1x and 4x syringeability samples. The concentration of each sample will be determined by summing the total peak area of all VEGF Trap peaks and quantified using a standard curve. A standard curve created by using different injection volumes of a VEGF Trap Standard at the same concentration as the formulation being tested will be used to determine the protein concentration. The standard will be formulated in the oncology formulation to the desired protein concentration. The concentration of the standard will be by uv-vis. The standard will be aliquoted into single use vials that are stored at -80 °C.

SE-HPLC: SE-HPLC will be performed on syringes #1-#4 and the vial at each time point including the 1x and 4x syringeability samples to detect and quantify molecular weight variants of VEGF Trap present in the stability samples. SE-HPLC will be performed using an Agilent 1100 HPLC system with a Pharmacia Superdex 200 HR 10/300 column attached. The method uses an isocratic 82 minute method with a flow rate of 0.3 mL/min and a 10 mM Phosphate pH 7.0 running buffer containing 500 mM NaCl. The signal will be monitored at 215nm. 20 μg of VEGF Trap from each sample will be analyzed. Percent purity will be calculated by taking the peak area for the native VEGF Trap peak divided by the total peak area for all VEGF Trap peaks observed and multiplied by 100.

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RP-HPLC: RP-HPLC will be performed on one of the three needle up pre-filled syringes (syringe 2) pulled at each time point to determine the chemical stability of VEGF Trap. RP-HPLC will be performed using an Agilent HPLC system with a Reliasil 1000Å C18 5 um 250 x 4.6mm column attached. Solvent A consists of 0.1% TFA in Water and solvent B consists of 0.1% TFA in Acetonitrile. The method has a flow rate of 1mL/min, column temperature controlled at 50°C, signal monitored at 214nm and the following gradient:

Time (min)	Solvent A	Solvent B
0.00	70.0 %	30.0 %
5.00	70.0 %	30.0 %
18.00	63.0%	37.0%
33.00	10.0 %	90.0 %
36.00	10.0 %	90.0 %
39.00	10.0 %	90.0 %
42.00	70.0 %	30.0 %
60.00	70.0 %	30.0 %

A standard curve at each VEGF Trap concentration (i.e., 10 mg/mL and 40 mg/mL) will be ran using a working standard as described in the Concentration (Recovery) section above. Percent purity will be calculated by taking the peak area for the native VEGF Trap peak divided by the total peak area for all VEGF trap peaks observed and multiplied by 100.

SDS-PAGE: SDS-PAGE (reduced and nonreduced) will be performed on a Novex Bis-Tris 4-12% 1.0 mm gel for one of the four needle up pre-filled syringes (syringe 3) pulled at the time points listed below to determine the chemical stability of VEGF Trap. The samples from a given time point for all devices will be analyzed on the same gel. The effects of the different devices on the stability of VEGF Trap will be performed by visually comparing the banding pattern for each sample. The time points to be tested are 37°C (14 and 30 day), 25°C (1, 3 ,6, 9, 12, 18, and 24 month), 5°C (1,3,6,9,12,18 and 24 month) and t=0 samples.

Isoquant®: Isoquant® will be performed by a modified protocol from the manufacturer to determine the amount of deamidation present in the stability samples for one of the three needle up pre-filled syringes (syringe 3) pulled at each time point for 37°C and 5°C. The Isoquant® protocol will be recorded in the study notebook. The Isoquant® Kit detects isoaspartic acid which is a product of the deamidation process in proteins. Isoaspartic acid is detected via Protein Isoaspartyl Methyltransferase (PMIT) catalyzed generation of S-adenosyl homocystine (SAH). The amount of isoaspartic acid present in a sample is quantified using a RP-HPLC method and is reported as millimoles of isoaspartic acid to moles of VEGF Trap.

FTIR: FTIR will be only performed on one of the four needle up pre-filled syringes (syringe 1) pulled at the 37°C 28 day sample and the 5°C 3, 12, and 24 month

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samples. This analysis will determine if storage in the different devices has any effect on the secondary structure of the protein.

Binding Assay: The binding assay will be performed by the QC group in Rensselaer on one of the needle up pre-filled syringes (syringe 5) pulled at 37°C 28 days and the 5°C 3, 12, and 24 month samples. This will determine if storage in the different devices has any effect on the binding affinity of VEGF Trap to VEGF.

Data Analysis:

All data will be kept in research notebooks. Original copies of gels, chromatograms, protocols, pull schedules etc. will be kept in the study file. When all analyses are complete the samples generated in the experiment may be destroyed.

Approvals:

The Study Coordinator, Study Director and Director of Formulation Development must approve this protocol. Any modifications to this protocol must be approved by the Study Director and Director of Formulation Development.

Study Coordinator	Date 1/16/06 1/17/06
Study Director Kenneth S Graham Kenneth S Graham 1/30/06	Date 1/16/06
Director, Formulation Development Daniel B Kuij Daniel B Kuij, 02-03-06	Date 01-16-06

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Graham Ex. 3

NOTEBOOK NO. 5088

ISSUED TO Megan Malone

ON February 20, 2003

DEPARTMENT FORM/FILL

RETURNED

EUREKA LAB BOOK, INC.

P.O. Box 150 • 110 Winter Street • Holyoke, Massachusetts 01041

Phone 413-534-5671 Fax 413-534-5672 Web www.eurekalabbook.com

GUIDELINES

1) This laboratory notebook is intended to be a permanent record of your work.

2) Entries should be made in permanent ink - do not use pencil.

3) The title should be accurately recorded when starting a page.

4) All data is to be recorded directly into the notebook. The inclusion of all elaborate details is preferable. Notes and calculations should not be done on loose paper. In the case of error, draw a single line through the incorrect data. Do not erase or use correction fluid. All corrections should be initialed and dated.

5) After entering your data, sign and date all entries. Witness or witnesses should sign and date each entry in the spaces provided. The witnesses must observe the work that is done and have sufficient knowledge to understand what they have read. Names of operators and witnesses present during any demonstration should be recorded.

6) This notebook, and all information recorded therein, are the exclusive property of the Company. All contents of this book are **strictly confidential.** It must be returned when completed, upon request, or upon termination of employment. It should be kept in a protected place to safeguard against loss. If the book is lost, the supervisor should be notified immediately, and a written report describing the circumstances should be submitted.

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RGN-EYLEA-BIOSIM-00474379

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Date of Final Entry: 01Oct2007	
Supervisor: Tim Neenan	
Department: FORM/FILL	
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Project No. N/A

TITLE Formulation of VEGF Trap to 40mg/mL w/ low endotoxin sucrose

Book No. 5688

From Page No. N/A

C2-5688-103-SPS 11/10/05

Purpose The purpose of this experiment is to formulate VegF Trap drug substance batch lot C05002M440 52.2mg/mL to 40mg/mL w/ 10mM phosphate, 40mM NaCl, 0.03% Polysorbate-20, 5% low endotoxin sucrose and at a pH of 6.25. The formulation will supply toxicology fill and ITV syringe studies

Materials

Pooling DS vessel RN 05-0494 RMR 05-06-012 Exp. 4/27/10
Stir bar cycle # E05-212 exp 2/10/06
pipette RN 04-0197 RMR 04-03-063 exp. 3/25/09
RM680 RN 04-0116 RMR 04-02-021 exp 1/22/09
RM681 RN 03-1425 RMR 04-02-014 exp 11/16/08
RM617 RN 03-0649 RMR 03-06-056 exp 4-15-07
Sucrose RN 05-0956 Low endotoxin Ferro-Pfanstiehl
10% P-20 exp 11/16/05 @ 1041hrs (notebook 5688 p92)
Buffer vessel 1LPC RN 05-0494 RMR 05-06-012 exp 4-27-10
Stir bar cycle # E05-212 exp 2-10-06
Millipak 60 RN 04-0361 RMR 04-03-072 exp 12/31/05
Sample tubing cycle E05-211 exp 2/10/06
1LPC RN 05-0494 RMR 05-06-012 exp 4/27/10
Pipette RN 05-0490 RMR 05-06-027 exp 6/10/10

Procedure

Batch lot: C05002M440
Bottle #: ~~1~~ 3 Amount: 746.8 g 52.2mg/mL

Date/time thaw began: 11/15/05 @ ~~0415~~ 0400 hrs 11/15/05 by mjm
Date/time thaw ended: 11/15/05 @ 1353 hrs by mjm

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SIGNATURE	DATE	WITNESSED & UNDERSTOOD BY	DATE
[signature]	12/14/05	A Gallucci	1/9/06

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CONFIDENTIAL RGN-EYLEA-BIOSIM-00474493

Project No. N/A

TITLE Formulation of VEGF Trap to 40mg/mL w/ low endotoxin sucrose

Book No. 5688

From Page No. 103

C2-5688-103-SPS

11/15/05

Procedure

Room: 349 Cleaning exp. 12/11/05

LFH ECN: 01081 Cleaning exp 11/22/05

Scale ecn: ~~ta~~ 7134 mjm 11/15/05

Tare of DS pooling vessel: 186.1g

70 ~~50~~ mL sample removed for Form/Dev mjm 11/15/05

0.0 g zero

186.1 g Tare wt. pooling DS vessel

Net weight pooled DS: 672.2g

mjm 11/15/05

11/15/05 N/A mjm

VEGF TRAP

VEGF Trap Drug Substance

Batch Lot Number: C05002M440 52.2 mg/mL

Store at: ≤ −20°C Fill Weight: 746.8 g

Bottle #: 3 I&D JWH 11/9/05

CAUTION: New Drug - Limited by Federal (or United States) law to investigational use.

Mfg. by: Regeneron Pharmaceuticals, Inc. Tarrytown, NY 10591

mjm 11/15/05

zero Net wt DS

Time mixing start: 1410hrs

Time mixing stop: 1415hrs

assume 1g=1mL

Net Weight DS mjm 11/15/05 Density DS Net Volume DS 11/15/05

672.2 g ~~X~~ ÷ 1 g/mL = 672.2 mL mjm ~~11/14/05~~ mjm 11/15/05 AcG 11/15/05

Net Volume DS DS concentration Total protein Target FDS concentration Target Volume FDS

672.2 mL X 52.2 mg/mL = 35088.84 mg ÷ 40 mg/mL = 877.2 mL mjm 11/15/05 AcG 11/15/05

Target FDS Volume Volume DS Buffer & WFI required

877.2 mL − 672.2 mL = 205.0 mL mjm 11/15/05 AcG 11/15/05

Target Volume FDS Density FDS = Target Weight FDS

877.2 mL X 1.031 g/mL = 904.4g mjm 11/15/05 AcG 11/15/05

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SIGNATURE	DATE	WITNESSED & UNDERSTOOD BY	DATE
[signature]	12/14/05	A Gallucci	1/9/06

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Project No. N/A

TITLE Formulation of VEGF Trap 40mg/mL w/low endotoxin sucrose

Book No. 5688

From Page No. 104 C2-5688-103-SPS 11/15/05

Procedure

component	composition	Buffer's WFI		Amount Required
RM680	0.000800 g/mL X	205.0 mL	=	0.164 g
RM681	0.001126 g/mL X	205.0 mL	=	0.231 g
		Target Volume FDS		
RM617	0.002338 g/mL X	877.2 mL	=	2.051 g
Sucrose	0.05 g/mL X	877.2 mL	=	43.860 g
10% P-20	0.003 g/mL X	877.2 mL	=	2.632 g
			Total:	48.938 g

11/15/05 mym Arb 11/15/05

Arb 11/15/05

Target FDS Weight		Net Weight		Target Weight Buffer
904.4 g	−	672.2 g	=	232.2 g

mym 11/15/05 Arb 11/15/05

Target Buffer Weight		Total Excipients		Total WFI in buffer
232.2 g	−	48.938	=	183.3 g

mym 11/15/05 Arb 11/15/05

Scale ECN: 9439

mym 11/15/05 ~~Amou~~

component	amount required	amount weighed
RM680	0.164 g	0.164 g
RM681	0.231 g	0.231 g
RM617	mym 11/15/05 ~~0~~.2.051 g	2.051 g
Sucrose	43.860 g	43.860 g
10% P-20	2.632 g	2.632 g

WFI Drop: 349 WFI 1

Scale ECN: 7134

Tare wt. of Buffer vessel w/ stir bar: 186.4 g

Amt. of WFI added to ~~Buffer~~ vessel: 183.3 g

0.0 g zero

186.4 g Buffer vessel w/ stir bar Tare wt.

0.0 g zero

183.3 g Amt of WFI added to Buffer vessel

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SIGNATURE	DATE	WITNESSED & UNDERSTOOD BY	DATE
[signature]	12/14/05	A Galluccio	1/9/06

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CONFIDENTIAL RGN-EYLEA-BIOSIM-00474495

Project No. N/A

TITLE ~~105~~ 106 Formulation of VEGF Trap to 40mg/mL Flow endotoxin sucrose Book No. 5688

From Page No. 105 C2-5488-103-SPS

Procedure

component	mix start	mix stop
RM680	1442 hrs	1447 hrs
RM681	1447 hrs	1452 hrs
RM617	1452 hrs	1457 hrs
Sucrose	1451 hrs	~~1402 hrs~~ 1502 hrs
10% P20	1502 ~~1402~~ hrs	1507 hrs

pH meter ecn: 13931
calibration exp: 11/16/05
pH = 6.40 @ 20.6°C by mym

1mL sample

Filtration of buffer into DS
Millipak 60 flushed with ~200mL of WFI then visually drained.
mix start time: 1522 hrs mix stop time: 1527 hrs

FDS pH = 6.36 @ 20.7 °C by mym

Gross wt.	Tare wt.	Net wt FDS
1082.9 g	186.1 g	896.8 g

mym 11/15/05

Samples removed from FDS for QC Chem + Micro.
15mL → QC Chem
12mL → Micro
3x1mL → Mfg retain

gross wt remaining	Tare Weight	Net weight 2-8°C vessel
500.0 g	186.1 g	313.9 g

mym 11/15/05

2-8°C vessel stored in 2-8°C in ECN 13875 @ 1547 hrs on 11/15/05
≤-40°C vessels store in ECN 13935 on 1420 hrs @ 11/15/05 ~~tac~~ mym 11/15/05

zero
gross wt
mym 11/15/05
11/15/05 AG
zero
Net wt. ves ≤-40°C to Vc
zero
Net wt. vessel ≤-40°C Form/DRV
11/15/05 AG
zero
Gross wt 2-8°C bottle

To Page No. N/A

SIGNATURE	DATE	WITNESSED & UNDERSTOOD BY	DATE
[signature]	12/14/05	A Gallucci	1/9/06

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Test Date : 11/15/2005 Time: 17:20

Record Data:

Product : C2-5488-103-SPS
Product Lot: 5488.04-03-072
Filter Type: Millipak 60
Filter Lot : exp 12/31/05
Setting Mpa: 3.0
Remarks :

Test Parameters:

Test Phase : Diag/Pum Syst.
S.P. min. : 50.00 psi
S.P. max. : 52.00 psi

Test Results:

S.P. : 51.41 psi
Inlet Volume : 127 ml

Evaluation:

Test passed

Signature A Gallucci 11/15/05

Graham Ex. 4

Stability Study VGFT-SS207 37ºC

Device	Length of stress (days) Theoretical	Length of stress (days) Actual	Syringe	HMW Peak Area	HMW Peak Area	HMW Peak Area	Native Peak Area	LMW Peak Area	LMW Peak Area	[VEGF-TRAP] mg/ml	% VEGF-TRAP Recov-ered	% Native VEGF-TRAP	% HMW Species	% LMW Species
#1	t=0	0	S1	0	0	549	80482	0	0	42.2	100.0	99.3	0.7	0.0
			S2	0	0	497	73534	0	0	38.4	100.0	99.3	0.7	0.0
			S3	0	0	499	76050	0	0	39.8	100.0	99.3	0.7	0.0
			S4	0	0	490	75245	0	0	39.3	100.0	99.4	0.6	0.0
			Avg	0	0	509	76328	0	0	39.9	100.0	99.3	0.7	0.0
	7	6.7	S1	0	56	1584	82413	334	198	41.4	103.6	97.4	1.9	0.6
			S2	0	51	1560	82753	258	152	41.5	103.8	97.6	1.9	0.5
			S3	0	42	1506	78320	377	258	39.4	98.6	97.3	1.9	0.8
			S4	0	50	1831	82623	348	283	41.6	104.2	97.0	2.2	0.7
			Avg	0	50	1620	81527	329	223	41.0	102.5	97.3	2.0	0.7
	14	13.7	S1	0	0	2686	74111	180	209	39.1	97.9	96.0	3.5	0.5
			S2	0	0	2657	74104	162	149	39.0	97.7	96.1	3.4	0.4
			S3	0	0	2701	73956	146	170	39.0	97.6	96.1	3.5	0.4
			S4	0	225	3029	72607	195	198	38.6	96.6	95.2	4.3	0.5
			Avg	0	56	2768	73695	171	182	38.9	97.5	95.9	3.7	0.5
	21	20.3	S1	0	214	3539	72122	255	298	39.8	99.7	94.4	4.9	0.7
			S2	0	190	3525	72718	219	228	40.1	100.3	94.6	4.8	0.6
			S3	0	184	3351	69697	232	263	38.4	96.2	94.5	4.8	0.7
			S4	0	239	3895	69263	221	247	38.5	96.3	93.8	5.6	0.6
			Avg	0	207	3578	70950	232	259	39.2	98.1	94.3	5.0	0.7
	28	27.7	S1	0	280	3673	73035	596	130	39.3	98.5	94.0	5.1	0.9
			S2	0	255	3689	71215	534	470	38.6	96.6	93.5	5.2	1.3
			S3	0	264	3776	72818	523	550	39.4	98.8	93.4	5.2	1.4
			S4	0	376	4622	71528	545	558	39.3	98.4	92.1	6.4	1.4
			Avg	0	294	3940	72149	550	427	39.2	98.1	93.3	5.5	1.3

Regeneron Ex. 2024
Formycon v. Regeneron
IPR2025-00233
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#2	t=0	0	S1	0	0	527	78972	0	0	41.4	100.0	99.3	0.7	0.0
			S2	0	0	478	74712	0	0	39.1	100.0	99.4	0.6	0.0
			S3	0	0	479	76710	0	0	40.1	100.0	99.4	0.6	0.0
			S4	0	0	478	76037	0	0	39.8	100.0	99.4	0.6	0.0
			Avg	0	0	491	76608	0	0	40.1	100.0	99.4	0.6	0.0
	7	6.7	S1	0	71	1620	78106	352	454	39.4	98.4	96.9	2.1	1.0
			S2	0	61	1570	77762	376	269	39.1	97.7	97.2	2.0	0.8
			S3	0	68	1747	82288	316	316	41.4	103.4	97.1	2.1	0.7
			S4	0	69	1808	78024	334	307	39.4	98.3	96.9	2.3	0.8
			Avg	0	67	1686	79045	345	337	39.8	99.4	97.0	2.2	0.8
	14	13.7	S1	0	0	2596	74226	161	167	39.1	97.5	96.2	3.4	0.4
			S2	0	0	2589	74608	164	241	39.3	98.1	96.1	3.3	0.5
			S3	0	0	2633	75752	177	204	39.9	99.6	96.2	3.3	0.5
			S4	0	226	3140	74805	172	217	39.8	99.3	95.2	4.3	0.5
			Avg	0	57	2740	74848	169	207	39.5	98.6	95.9	3.6	0.5
	21	20.3	S1Seinj	0	250	3330	65077	186	217	36.0	89.7	94.2	5.2	0.6
			S2	0	223	3592	71776	218	225	39.6	98.9	94.4	5.0	0.6
			S3	0	219	3530	71313	214	231	39.3	98.2	94.4	5.0	0.6
			S4	0	275	4306	70159	271	314	39.2	97.9	93.1	6.1	0.8
			Ave	0	242	3690	69581	222	247	38.5	96.2	94.1	5.3	0.6
	28	27.7	S1	0	354	3826	72811	571	566	39.5	98.7	93.2	5.4	1.5
			S2	0	342	3916	73669	622	661	40.1	100.0	93.0	5.4	1.6
			S3	0	268	3804	71621	510	480	38.8	96.9	93.4	5.3	1.3
			S4	0	394	4536	68790	498	408	37.9	94.5	92.2	6.6	1.2
			Avg	0	340	4021	71723	550	529	39.1	97.5	92.9	5.7	1.4

#3	t=0	0	S1	0	0	498	78967	0	0	41.3	100.0	99.4	0.6	0.0
			S2	0	0	451	74099	0	0	38.7	100.0	99.4	0.6	0.0
			S3	0	0	472	75574	0	0	39.5	100.0	99.4	0.6	0.0
			S4	0	0	482	75293	0	0	39.4	100.0	99.4	0.6	0.0
			Avg	0	0	476	75983	0	0	39.7	100.0	99.4	0.6	0.0
	7	6.7	S1	0	58	1623	78067	313	213	39.3	98.8	97.3	2.1	0.7
			S2	0	67	1646	77837	260	234	39.2	98.5	97.2	2.1	0.6
			S3	0	63	1659	78904	287	316	39.7	100.0	97.1	2.1	0.7
			S4	0	68	1804	77740	345	349	39.3	98.8	96.8	2.3	0.9
			Avg	0	64	1683	78137	301	278	39.4	99.0	97.1	2.2	0.7
	14	13.7	S1	0	0	2632	74346	165	183	39.2	98.5	96.1	3.4	0.5
			S2	0	0	2566	73218	180	358	38.6	97.2	95.9	3.4	0.7
			S3	0	0	2599	73919	168	252	39.0	98.0	96.1	3.4	0.5
			S4	0	0	2985	72910	177	229	38.6	97.2	95.6	3.9	0.5
			Avg	0	0	2696	73598	173	256	38.8	97.8	95.9	3.5	0.6
	21	20.3	S1	0	226	3591	72179	215	249	39.8	100.3	94.4	5.0	0.6
			S2	0	178	3585	71720	254	282	39.6	99.7	94.3	5.0	0.7
			S3	0	203	3394	69566	225	275	38.4	96.6	94.4	4.9	0.7
			S4	0	283	4057	69501	229	243	38.7	97.4	93.5	5.8	0.6
			Avg	0	223	3657	70742	231	262	39.1	98.5	94.2	5.2	0.7
	28	27.7	S1	0	280	4032	73398	549	480	39.8	100.2	93.2	5.5	1.3
			S2	0	301	4042	72703	470	534	39.5	99.4	93.1	5.6	1.3
			S3	0	317	3968	70884	527	660	38.7	97.4	92.8	5.6	1.6
			S4	0	406	4762	71249	530	706	39.3	98.9	91.8	6.7	1.6
			Avg	0	326	4201	72059	519	595	39.3	99.0	92.7	5.8	1.4

#4	t=0	0	S1	0	0	532	79812	0	0	41.8	100.0	99.3	0.7	0.0
			S2	0	0	464	75433	0	0	39.4	100.0	99.4	0.6	0.0
			S3	0	0	486	75338	0	0	39.4	100.0	99.4	0.6	0.0
			S4	0	0	503	76975	0	0	40.3	100.0	99.4	0.6	0.0
			Avg	0	0	496	76890	0	0	40.2	100.0	99.4	0.6	0.0
	7	6.7	S1	0	62	1688	78507	318	257	39.5	98.3	97.1	2.2	0.7
			S2	0	58	1687	78329	311	237	39.4	98.0	97.2	2.2	0.7
			S3	0	93	1750	79755	291	339	40.2	100.0	97.0	2.2	0.8
			S4	0	65	1869	78018	336	367	39.4	98.1	96.7	2.4	0.9
			Avg	0	70	1749	78652	314	300	39.7	98.6	97.0	2.2	0.8
	14	13.7	S1	0	174	2699	74110	157	172	39.2	97.3	95.9	3.7	0.4
			S2	0	257	2757	74477	271	706	39.8	98.8	94.9	3.8	1.2
			S3	16	203	2697	73965	230	334	39.2	97.5	95.5	3.8	0.7
			S4	0	212	3058	75036	175	189	39.9	99.1	95.4	4.2	0.5
			Avg	4	212	2803	74397	208	350	39.5	98.2	95.4	3.9	0.7
	21	20.3	S1	0	234	3659	74105	238	290	40.9	101.7	94.4	5.0	0.7
			S2	0	194	3609	72575	240	280	40.1	99.6	94.4	4.9	0.7
			S3	0	218	3458	70459	217	260	38.9	96.6	94.4	4.9	0.6
			S4	0	330	4342	71545	236	292	40.0	99.4	93.2	6.1	0.7
			Avg	0	244	3767	72171	233	281	40.0	99.3	94.1	5.2	0.7
	28	27.7	S1	0	331	4161	73540	503	618	40.0	99.5	92.9	5.7	1.4
			S2	0	309	4144	72654	500	615	39.6	98.4	92.9	5.7	1.4
			S3	0	333	4195	72742	489	590	39.6	98.5	92.8	5.8	1.4
			S4	0	442	4826	69925	513	656	38.7	96.2	91.6	6.9	1.5
			Avg	0	354	4332	72215	501	620	39.5	98.2	92.6	6.0	1.4

#5	t=0	0	S1	0	0	509	79339	0	0	41.5	100.0	99.4	0.6	0.0
			S2	0	0	492	75410	0	0	39.4	100.0	99.4	0.6	0.0
			S3	0	0	530	77056	0	0	40.3	100.0	99.3	0.7	0.0
			S4	0	0	474	75743	0	0	39.6	100.0	99.4	0.6	0.0
			Avg	0	0	501	76887	0	0	40.2	100.0	99.4	0.6	0.0
	7	6.7	S1	0	89	1697	77666	365	261	39.2	97.4	97.0	2.2	0.8
			S2	0	79	1738	79375	309	323	40.0	99.5	97.0	2.2	0.8
			S3	0	52	1715	80574	309	170	40.5	100.7	97.3	2.1	0.6
			S4	0	65	1881	77634	304	315	39.2	97.5	96.8	2.4	0.8
			Avg	0	71	1758	78812	322	267	39.7	98.7	97.0	2.3	0.7
	14	13.7	S1	0	166	2638	74171	178	191	39.2	97.4	95.9	3.6	0.5
			S2	0	164	2574	71841	171	165	37.9	94.2	95.9	3.7	0.4
			S3	0	162	2654	74799	167	181	39.5	98.2	95.9	3.6	0.4
			S4	0	0	3193	72907	176	195	38.7	96.2	95.3	4.2	0.5
			Avg	0	123	2765	73430	173	183	38.8	96.5	95.8	3.8	0.5
	21	20.3	S1	0	234	3628	73457	219	252	40.5	100.8	94.4	5.0	0.6
			S2	0	211	3627	70508	237	266	39.0	96.9	94.2	5.1	0.7
			S3	0	209	3594	71557	263	311	39.6	98.3	94.2	5.0	0.8
			S4	0	301	4540	70942	267	302	39.8	98.9	92.9	6.3	0.7
			Avg	0	239	3847	71616	247	283	39.7	98.7	93.9	5.4	0.7
	28	27.7	S1	0	330	4415	75714	505	588	41.2	102.4	92.8	5.8	1.3
			S2	0	327	4179	71227	459	463	38.8	96.5	92.9	5.9	1.2
			S3	0	366	4184	72082	491	529	39.3	97.7	92.8	5.9	1.3
			S4	0	557	5078	70789	596	755	39.4	97.9	91.0	7.2	1.7
			Avg	0	395	4464	72453	513	584	39.7	98.6	92.4	6.2	1.4

#6	t=0	0	S1	0	0	598	80845	0	0	42.4	100.0	99.3	0.7	0.0
			S2	0	0	510	74541	0	0	39.0	100.0	99.3	0.7	0.0
			S3	0	0	549	74683	0	0	39.1	100.0	99.3	0.7	0.0
			S4	0	0	497	75679	0	0	39.6	100.0	99.3	0.7	0.0
			Avg	0	0	539	76437	0	0	40.0	100.0	99.3	0.7	0.0
	7	6.7	S1	0	53	1758	78263	322	252	39.4	98.6	97.0	2.2	0.7
			S2	0	71	1867	79475	298	265	40.1	100.2	96.9	2.4	0.7
			S3	0	44	1772	79657	315	236	40.1	100.3	97.1	2.2	0.7
			S4	0	49	1745	78306	294	229	39.4	98.6	97.1	2.2	0.6
			Avg	0	54	1786	78925	307	246	39.8	99.4	97.1	2.3	0.7
	14	13.7	S1	0	151	2612	76358	183	247	40.3	100.8	96.0	3.5	0.5
			S2	0	154	2558	73559	158	199	38.8	97.0	96.0	3.5	0.5
			S3	0	0	2584	74892	115	192	39.4	98.5	96.3	3.3	0.4
			S4	0	196	3070	74207	168	204	39.4	98.5	95.3	4.2	0.5
			Avg	0	125	2706	74754	156	211	39.5	98.7	95.9	3.6	0.5
	21	20.3	S1	0	190	3105	67692	254	437	37.3	93.3	94.4	4.6	1.0
			S2	0	201	3525	72336	288	313	39.9	99.8	94.4	4.9	0.8
			S3	0	191	3374	69648	209	234	38.4	95.9	94.6	4.8	0.6
			S4	0	374	4353	69422	355	404	39.0	97.5	92.7	6.3	1.0
			Avg	0	239	3589	69775	277	347	38.7	96.6	94.0	5.2	0.8
	28	27.7	S1	0	322	4254	73656	442	420	40.0	100.0	93.1	5.8	1.1
			S2	0	311	4298	73602	465	494	40.0	100.1	93.0	5.8	1.2
			S3	0	324	4108	70959	449	482	38.7	96.7	93.0	5.8	1.2
			S4	0	374	4895	70030	473	483	38.6	96.6	91.8	6.9	1.3
			Avg	0	333	4389	72062	457	470	39.3	98.3	92.7	6.1	1.2

#7	t=0	0	S1	0	0	412	77578	0	0	40.6	100.0	99.5	0.5	0.0
			S2	0	0	376	76712	0	0	40.1	100.0	99.5	0.5	0.0
			Avg	0	0	394	77145	0	0	40.3	100.0	99.5	0.5	0.0
	7	6.7	S1	0	77	1742	77056	348	395	38.9	96.6	96.8	2.3	0.9
			S2	0	55	1741	77411	333	289	39.0	96.9	97.0	2.2	0.8
			Avg	0	66	1742	77234	341	342	39.0	96.7	96.9	2.3	0.9
	14	13.7	S1	0	206	2997	73462	136	203	39.0	96.7	95.4	4.2	0.4
			S2	0	224	3009	73201	135	267	38.9	96.5	95.3	4.2	0.5
			Avg	0	215	3003	73332	136	235	38.9	96.6	95.3	4.2	0.5
	21	20.3	S1	0	258	3851	71867	242	315	39.9	98.9	93.9	5.4	0.7
			S2	0	338	4239	70371	333	718	39.6	98.2	92.6	6.0	1.4
			Avg	0	298	4045	71119	288	517	39.7	98.6	93.2	5.7	1.1
	28	27.7	S1	0	424	4770	72580	458	536	39.8	98.8	92.1	6.6	1.3
			S2	0	439	4678	70954	511	722	39.1	97.1	91.8	6.6	1.6
			Avg	0	432	4724	71767	485	629	39.5	98.0	92.0	6.6	1.4

t=0 seq 060117F
t=7d seq 060120E
t=14d seq 060128G
t=21d seq 060206F
t=28d seq 060214G
Reinjected samples
D2S1 21D from seq 060222X

Stability Study VGFT-SS207 5ºC

Device	Length of stress (months) Theoretical	Length of stress (months) Actual	Syringe	HMW Peak Area	HMW Peak Area	HMW Peak Area	Native Peak Area	LMW Peak Area	LMW Peak Area	[VEGF-TRAP] mg/ml	% VEGF-TRAP Recov-ered	% Native VEGF-TRAP	% HMW Species	% LMW Species
#1	t=0	**0.0**	S1	0	0	549	80482	0	0	42.18	100.0	**99.32**	0.68	0.00
			S2	0	0	497	73534	0	0	38.44	100.0	**99.33**	0.67	0.00
			S3	0	0	499	76050	0	0	39.78	100.0	**99.35**	0.65	0.00
			S4	0	0	490	75245	0	0	39.35	100.0	**99.35**	0.65	0.00
			Avg	0	0	509	76328	0	0	39.94	100.0	**99.34**	0.66	0.00
	0.5	**0.5**	S1	0	0	567	80461	38	0	41.12	102.9	**99.25**	0.70	0.05
			S2	0	0	596	76360	65	0	39.00	97.7	**99.14**	0.77	0.08
			S3	0	0	560	79171	0	0	40.42	101.2	**99.30**	0.70	0.00
			S4	0	0	513	75830	0	0	38.65	96.8	**99.33**	0.67	0.00
			Avg	0	0	559	77956	26	0	39.79	99.6	**99.26**	0.71	0.03
	1m	**1.0**	S1	0	0	521	79196	0	0	40.30	100.9	**99.35**	0.65	0.00
			S2	0	0	505	77955	0	0	39.70	99.4	**99.36**	0.64	0.00
			S3	0	0	502	78469	0	0	39.94	100.0	**99.36**	0.64	0.00
			S4	0	0	497	78218	0	0	39.82	99.7	**99.37**	0.63	0.00
			Avg	0	0	506	78460	0	0	39.94	100.0	**99.36**	0.64	0.00
	2m	**2.1**	S1	0	0	639	76701	158	151	38.89	97.4	**98.78**	0.82	0.40
			S2	0	0	632	75938	114	110	38.47	96.3	**98.89**	0.82	0.29
			S3	0	0	566	74254	153	0	37.56	94.1	**99.04**	0.75	0.20
			S4	0	0	627	75103	95	146	38.06	95.3	**98.86**	0.83	0.32
			Avg	0	0	616	75499	130	102	38.24	95.8	**98.89**	0.81	0.30
	3m	**3.0**	S1	0	0	723	75490	111	0	40.29	100.9	**98.91**	0.95	0.15
			S2	**vial broken; no sample**										
			S3	0	0	683	73701	119	0	39.28	98.4	**98.92**	0.92	0.16
			S4	0	0	786	74766	83	0	39.91	99.9	**98.85**	1.04	0.11
			Avg	0	0	731	74652	104	0	39.82	99.7	**98.89**	0.97	0.14
	4m	**3.9**	S1	0	0	736	80983	0	0	39.61	99.2	**99.10**	0.90	0.00
			S2	0	0	680	78387	0	0	38.32	96.0	**99.14**	0.86	0.00
			S3	0	0	738	81003	0	0	39.62	99.2	**99.10**	0.90	0.00
			S4	0	0	711	79211	0	0	38.74	97.0	**99.11**	0.89	0.00
			Avg	0	0	716	79896	0	0	39.07	97.8	**99.11**	0.89	0.00
	5m	**4.9**	S1	0	0	640	75096	96	0	39.63	99.2	**99.03**	0.84	0.13
			S2	0	0	582	74742	93	0	39.41	98.7	**99.10**	0.77	0.12
			S3	0	0	585	73448	0	0	38.70	96.9	**99.21**	0.79	0.00
			S4	0	0	553	73176	0	0	38.54	96.5	**99.25**	0.75	0.00
			Avg	0	0	590	74116	47	0	39.07	97.8	**99.15**	0.79	0.06
	6m	**6.0**	S1	0	0	673	76717	135	0	39.55	99.0	**98.96**	0.87	0.17
			S2	0	0	649	76239	109	0	39.28	98.3	**99.02**	0.84	0.14
			S3	0	0	646	75834	0	0	39.00	97.7	**99.16**	0.84	0.00
			S4	0	0	653	76865	101	0	39.60	99.2	**99.03**	0.84	0.13
			Avg	0	0	655	76414	86	0	39.36	98.6	**99.04**	0.85	0.11
	9m	**9.0**	S1	0	0	781	82952	0	0	40.16	100.6	**99.07**	0.93	0.00
			S2	0	0	746	79541	0	0	38.46	96.3	**99.07**	0.93	0.00
			S3	0	0	729	78764	0	0	38.07	95.3	**99.08**	0.92	0.00
			S4	0	0	767	78857	132	0	38.20	95.6	**98.87**	0.96	0.17
			Avg	0	0	756	80029	33	0	38.72	97.0	**99.02**	0.94	0.04
	12m	**12.0**	S1	0	0	788	75042	90	0	39.03	97.7	**98.84**	1.04	0.12
			S2	0	0	768	75620	109	0	39.34	98.5	**98.85**	1.00	0.14
			S3	0	0	824	75126	109	0	39.11	97.9	**98.77**	1.08	0.14
			S4	0	0	839	76085	197	0	39.67	99.3	**98.66**	1.09	0.26
			Avg	0	0	805	75468	126	0	39.29	98.4	**98.78**	1.05	0.17
	15m	**15.0**	S1	0	31	840	76571	231	142	36.49	91.4	**98.40**	1.12	0.48
			S2	0	22	832	77924	263	190	37.18	93.1	**98.35**	1.08	0.57
			S3	0	48	842	77679	233	137	37.04	92.7	**98.40**	1.13	0.47
			S4	0	43	862	79111	255	154	37.76	94.5	**98.37**	1.13	0.51
			Avg	0	36	844	77821	246	156	37.12	92.9	**98.38**	1.11	0.51
	18m	**17.9**	S1	0	87	966	82684	152	84	41.99	105.1	**98.47**	1.26	0.27
			S2	0	47	910	80704	138	121	40.95	102.5	**98.52**	1.17	0.32
			S3	0	83	923	80939	117	82	41.06	102.8	**98.53**	1.22	0.24
			S4	0	0	999	80113	142	55	40.64	101.8	**98.53**	1.23	0.24
			Avg	0	54	950	81110	137	86	41.16	103.1	**98.51**	1.22	0.27
	24m	**24.0**	S1	0	0	860296	75578117	16103	13969	42.03	105.2	**98.84**	1.13	0.04
			S2	0	0	822486	72732394	8758	24713	40.45	101.3	**98.84**	1.12	0.05
			S3	0	0	801320	72256199	13757	19464	40.18	100.6	**98.86**	1.10	0.05
			S4	0	0	839415	73554979	17000	19281	40.91	102.4	**98.82**	1.13	0.05
			Avg	0	0	830879	73530422	13905	19357	40.89	102.4	**98.84**	1.12	0.05
	31m	**31.1**	S1 up							38.54	96.5	**98.45**	1.40	0.15
			S2 up							38.33	96.0	**98.54**	1.35	0.11
			S3 horiz							39.74	99.5	**97.62**	2.18	0.20
			S4 down							39.63	99.2	**98.53**	1.39	0.08
			Avg							39.06	97.8	**98.29**	1.58	0.14
	31m rpt	**31.1**	S3 horiz							39.50	98.9	**97.70**	2.14	0.16
	32m	**31.8**	Horizontal 1							40.44	101.3	**97.80**	1.99	0.21
			Horizontal 2							36.88	92.3	**98.05**	1.81	0.14
	36	**36.0**	S1							40.13	100.5	**98.4**	1.38	0.22
			S2							40.218	100.7	**98.34**	1.4	0.26
			S3							40.101	100.4	**98.4**	1.36	0.24
			S4							39.6	99.2	**98.37**	1.37	0.26
			Avg							40.01	100.19	**98.38**	1.38	0.25

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#2	t=0	**0**	S1	0	0	527	78972	0	0	41.36	100.0	**99.34**	0.66	0.00	
			S2	0	0	478	74712	0	0	39.06	100.0	**99.36**	0.64	0.00	
			S3	0	0	479	76710	0	0	40.13	100.0	**99.38**	0.62	0.00	
			S4	0	0	478	76037	0	0	39.77	100.0	**99.38**	0.62	0.00	
			Avg	0	0	491	76608	0	0	40.08	100.0	**99.36**	0.64	0.00	
	0.5	**0.5**	S1	0	0	532	77893	0	0	39.73	99.1	**99.32**	0.68	0.00	
			S2	0	0	516	77185	0	0	39.36	98.2	**99.34**	0.66	0.00	
			S3	0	0	532	77713	0	0	39.64	98.9	**99.32**	0.68	0.00	
			S4	0	0	567	77250	96	0	39.47	98.5	**99.15**	0.73	0.12	
			Avg	0	0	537	77510	24	0	39.55	98.7	**99.28**	0.69	0.03	
	1m	**1**	S1	0	0	479	77996	0	0	39.71	99.1	**99.39**	0.61	0.00	
			S2	0	0	498	78788	0	0	40.10	100.0	**99.37**	0.63	0.00	
			S3	0	0	454	77407	0	0	39.41	98.3	**99.42**	0.58	0.00	
			S4	0	0	581	77949	0	0	39.52	98.6	**99.26**	0.74	0.00	re-run on seq i
			Avg	0	0	503	78035	0	0	39.74	99.2	**99.36**	0.64	0.00	
	2m	**2.1**	S1	0	0	567	76080	90	48	38.46	96.0	**99.08**	0.74	0.18	
			S2	0	0	549	75211	73	37	38.01	94.8	**99.13**	0.72	0.14	
			S3	0	0	612	74837	127	0	37.86	94.5	**99.02**	0.81	0.17	
			S4	0	0	616	79369	0	0	40.27	100.5	**99.23**	0.77	0.00	re-run on seq i
			Avg	0	0	586	76374	73	21	38.60	96.3	**99.12**	0.76	0.12	
	3m	**3**	S1	0	0	657	76384	115	0	40.75	101.7	**99.00**	0.85	0.15	
			S2	0	69	739	84869	235	36	40.99	102.3	**98.74**	0.94	0.32	
			S3	0	0	610	72680	70	0	38.65	96.4	**99.07**	0.83	0.10	
			S4	0	0	725	73504	136	0	39.21	97.8	**98.84**	0.97	0.18	
			Avg	0	17	683	76859	139	9	41.05	102.4	**98.91**	0.90	0.19	
	4m	**3.9**	S1	0	0	724	82858	0	0	40.52	101.1	**99.13**	0.87	0.00	
			S2	0	0	646	78854	0	0	38.53	96.1	**99.19**	0.81	0.00	
			S3	0	0	687	80695	0	0	39.45	98.4	**99.16**	0.84	0.00	
			S4	0	0	667	79599	0	0	38.91	97.1	**99.17**	0.83	0.00	
			Avg	0	0	667	79599	0	0	38.91	97.1	**99.17**	0.83	0.00	
	5m	**4.9**	S1	0	0	596	75077	194	0	39.64	98.9	**98.96**	0.79	0.26	
			S2	0	0	583	74748	124	0	39.43	98.4	**99.06**	0.77	0.16	
			S3	0	0	570	74614	0	0	39.29	98.0	**99.24**	0.76	0.00	
			S4	0	0	570	74453	0	0	39.21	97.8	**99.24**	0.76	0.00	
			Avg	0	0	580	74723	80	0	39.39	98.3	**99.13**	0.77	0.11	
	6m	**6**	S1	0	0	643	77523	88	0	39.94	99.7	**99.07**	0.82	0.11	
			S2	0	0	634	74156	83	0	38.15	95.2	**99.04**	0.85	0.11	
			S3	0	0	629	76154	99	0	39.21	97.8	**99.05**	0.82	0.13	
			S4	0	0	645	77353	95	0	39.85	99.4	**99.05**	0.83	0.12	
			Avg	0	0	638	76297	91	0	39.29	98.0	**99.05**	0.83	0.12	
	9m	**9**	S1	0	0	934	83188	244	0	40.47	101.0	**98.60**	1.11	0.29	
			S2	0	0	695	77310	104	0	37.38	93.3	**98.98**	0.89	0.13	
			S3	0	0	858	77482	289	0	37.64	93.9	**98.54**	1.09	0.37	
			S4	0	0	726	78582	160	0	38.05	95.0	**98.89**	0.91	0.20	
			Avg	0	0	803	79141	199	0	38.39	95.8	**98.75**	1.00	0.25	
	12m	**12**	S1	0	0	789	75835	40	0	39.43	98.4	**98.92**	1.03	0.05	
			S2	0	0	766	75161	57	0	39.07	97.5	**98.92**	1.01	0.08	
			S3	0	0	743	75156	87	0	39.07	97.5	**98.91**	0.98	0.11	
			S4	0	0	772	78447	66	0	40.82	101.8	**98.94**	0.97	0.08	
			Avg	0	0	768	76150	63	0	39.60	98.8	**98.92**	1.00	0.08	
	15m	**15**	S1	0	37	823	76258	201	71	36.29	90.5	**98.54**	1.11	0.35	
			S2	0	31	835	78112	284	117	37.25	92.9	**98.40**	1.09	0.51	
			S3	0	34	858	78127	209	71	37.21	92.9	**98.52**	1.12	0.35	
			S4	0	48	849	78236	380	585	37.60	93.8	**97.68**	1.12	1.20	
			Avg	0	38	841	77683	269	211	37.09	92.5	**98.28**	1.11	0.61	
	18m	**17.9**	S1	0	0	902	80020	98	46	40.52	101.1	**98.71**	1.11	0.18	
			S2	0	83	906	78232	128	94	39.70	99.0	**98.48**	1.24	0.28	
			S3	0	74	878	79898	125	74	40.51	101.1	**98.58**	1.17	0.25	
			S4	0	81	871	80036	111	77	40.57	101.2	**98.60**	1.17	0.23	
			Avg	0	60	889	79547	116	73	40.32	100.6	**98.59**	1.18	0.23	
	24m	**24**	S1	0	0	837222	74587582	9278	23463	41.48	103.5	**98.85**	1.11	0.04	
			S2	0	0	828931	73685065	13106	24799	40.98	102.2	**98.84**	1.11	0.05	
			S3	0	0	824788	73256990	15229	25695	40.74	101.7	**98.83**	1.11	0.06	
			S4	0	0	786743	71187138	16372	17803	39.58	98.8	**98.86**	1.09	0.05	
			Avg	0	0	819421	73179194	13496	22940	40.69	101.5	**98.85**	1.11	0.05	
	31m	**31.1**	S1 up							37.70	94.1	**98.50**	1.39	0.11	
			S2 up							37.51	93.6	**98.58**	1.34	0.08	
			S3 horiz							40.17	100.2	**95.15**	4.62	0.23	
			S4 down							39.18	97.8	**98.63**	1.29	0.07	
			Avg*							38.64	96.4	**98.57**	2.16	0.12	
	31m rpt	**31.1**	S3 horiz							39.86	99.5	**95.12**	4.67	0.22	
	32m	**31.8**	Horizontal 1							40.75	101.7	**95.76**	3.99	0.25	
			Horizontal 2							37.98	94.8	**95.17**	4.59	0.25	
	36	**36**	S1							39.768	99.2	**98.49**	1.32	0.2	
			S2							40.506	101.1	**98.48**	1.3	0.21	
			S3							39.963	99.7	**98.53**	1.33	0.14	
			S4							40.105	100.1	**98.58**	1.3	0.12	
			Avg							40.09	100.02	**98.52**	1.31	0.17	

#3	t=0	**0**	S1	0	0	498	78967	0	0	41.34	100.0	**99.37**	0.63	0.00
			S2	0	0	451	74099	0	0	38.72	100.0	**99.40**	0.60	0.00
			S3	0	0	472	75574	0	0	39.51	100.0	**99.38**	0.62	0.00
			S4	0	0	482	75293	0	0	39.37	100.0	**99.36**	0.64	0.00
			Avg	0	0	476	75983	0	0	39.74	100.0	**99.38**	0.62	0.00
	0.5	**0.5**	S1	0	0	575	79512	0	0	40.60	102.2	**99.28**	0.72	0.00
			S2	0	0	526	76157	0	0	38.82	97.7	**99.31**	0.69	0.00
			S3	0	0	546	78271	0	0	39.94	100.5	**99.31**	0.69	0.00
			S4	0	0	509	76468	0	0	38.98	98.1	**99.34**	0.66	0.00
			Avg	0	0	539	77602	0	0	39.59	99.6	**99.31**	0.69	0.00
	1m	**1**	S1	0	0	529	79295	0	0	40.35	101.6	**99.34**	0.66	0.00
			S2	0	0	472	77937	0	0	39.68	99.8	**99.40**	0.60	0.00
			S3	0	0	476	78059	0	0	39.74	100.0	**99.39**	0.61	0.00
			S4	0	0	470	76353	0	0	38.91	97.9	**99.39**	0.61	0.00
			Avg	0	0	487	77911	0	0	39.67	99.8	**99.38**	0.62	0.00
	2m	**2.1**	S1	0	0	582	78361	72	33	39.58	99.6	**99.13**	0.74	0.13
			S2	0	0	551	75172	64	41	37.99	95.6	**99.13**	0.73	0.14
			S3	0	0	554	75497	72	39	38.15	96.0	**99.13**	0.73	0.15
			S4	0	0	546	75194	56	21	37.98	95.6	**99.18**	0.72	0.10
			Avg	0	0	558	76056	66	34	38.43	96.7	**99.14**	0.73	0.13
	3m	**3**	S1	0	0	652	75319	93	0	40.14	101.0	**99.02**	0.86	0.12
			S2	0	92	716	83593	201	69	40.38	101.6	**98.73**	0.95	0.32
			S3	0	0	653	72855	0	0	38.73	97.5	**99.11**	0.89	0.00
			S4	0	0	766	75001	85	0	40.03	100.7	**98.88**	1.01	0.11
			Avg	0	23	697	76692	95	17	40.95	103.1	**98.93**	0.93	0.14
	4m	**3.9**	S1	0	0	726	83995	0	0	41.07	103.4	**99.14**	0.86	0.00
			S2	0	0	704	80201	0	0	39.22	98.7	**99.13**	0.87	0.00
			S3	0	0	706	80195	0	0	39.22	98.7	**99.13**	0.87	0.00
			S4	0	0	706	80357	0	0	39.29	98.9	**99.13**	0.87	0.00
			Avg	0	0	711	81187	0	0	39.70	99.9	**99.13**	0.87	0.00
	5m	**4.9**	S1	0	0	602	74519	0	0	39.26	98.8	**99.20**	0.80	0.00
			S2	0	0	553	75245	124	0	39.67	99.8	**99.11**	0.73	0.16
			S3	0	0	576	74028	142	0	39.07	98.3	**99.04**	0.77	0.19
			S4	0	0	576	74086	91	0	39.07	98.3	**99.11**	0.77	0.12
			Avg	0	0	577	74470	89	0	39.27	98.8	**99.11**	0.77	0.12
	6m	**6**	S1	0	0	690	77791	91	0	40.11	100.9	**99.01**	0.88	0.12
			S2	0	0	629	75821	65	0	39.02	98.2	**99.09**	0.82	0.08
			S3	0	0	662	76706	116	0	39.53	99.5	**99.00**	0.85	0.15
			S4	0	0	673	78504	79	0	40.47	101.8	**99.05**	0.85	0.10
			Avg	0	0	664	77206	88	0	39.78	100.1	**99.04**	0.85	0.11
	9m	**9**	S1	0	0	792	83025	92	0	40.24	101.3	**98.95**	0.94	0.11
			S2	0	0	707	79747	0	0	38.54	97.0	**99.12**	0.88	0.00
			S3	0	0	714	78480	107	0	37.97	95.6	**98.96**	0.90	0.13
			S4	0	0	833	78996	283	0	38.37	96.6	**98.61**	1.04	0.35
			Avg	0	0	762	80062	121	0	38.78	97.6	**98.91**	0.94	0.15
	12m	**12**	S1	0	0	743	75273	90	0	39.13	98.5	**98.91**	0.98	0.12
			S2	0	0	724	73885	84	0	38.38	96.6	**98.92**	0.97	0.11
			S3	0	0	730	74566	124	0	38.77	97.6	**98.87**	0.97	0.16
			S4	0	0	700	73225	0	0	37.98	95.6	**99.05**	0.95	0.00
			Avg	0	0	724	74237	75	0	38.56	97.1	**98.94**	0.97	0.10
	15m	**15**	S1	0	0	901	84814	0	0	39.62	99.7	**98.95**	1.05	0.00
			S2	0	0	855	81451	0	0	38.04	95.7	**98.96**	1.04	0.00
			S3	0	0	913	84174	0	0	39.33	99.0	**98.93**	1.07	0.00
			S4	0	0	882	82154	0	0	38.38	96.6	**98.94**	1.06	0.00
			Avg	0	0	888	83148	0	0	38.85	97.8	**98.94**	1.06	0.00

18m	**17.9**	S1	0	96	921	81222	117	53	41.20	103.7	**98.56**	1.23	0.21
		S2	0	109	904	78413	126	68	39.79	100.1	**98.48**	1.27	0.24
		S3	0	87	887	77314	121	93	39.22	98.7	**98.49**	1.24	0.27
		S4	0	116	839	77953	110	52	39.51	99.4	**98.59**	1.21	0.20
		Avg	0	102	888	78726	119	67	39.93	100.5	**98.53**	1.24	0.23
24m	**24**	S1	0	0	828751	75136610	13540	15296	41.77	105.1	**98.87**	1.09	0.04
		S2	NA	NA	NA	NA	NA	NA	NA	#VALUE!	**NA**	NA	NA
		S3	NA	NA	NA	NA	NA	NA	NA	#VALUE!	**NA**	NA	NA
		S4	0	0	813261	73187289	14032	19082	40.69	102.4	**98.86**	1.10	0.04
		Avg	0	0	821006	74161950	13786	17189	41.23	103.8	**98.87**	1.10	0.04
31m	**31.1**	S1 up							39.03	98.2	**98.59**	1.33	0.08
		S2 horiz							37.60	94.6	**76.55**	23.02	0.43
		S3 horiz							38.64	97.2	**80.91**	18.82	0.27
		S4 down							38.34	96.5	**98.63**	1.30	0.08
		Avg*							38.40	96.6	**98.61**	11.12	0.22
31m **rpt**	**31.1**	S2 horiz							39.49	99.4	**76.90**	22.82	0.28
		S3 horiz							40.38	101.6	**80.96**	18.78	0.27
31m	**31.8**	S5 horiz							39.63	99.7	**86.75**	12.98	0.27
		S6 horiz							40.07	100.8	**84.30**	15.22	0.48
		S7 horiz							40.58	102.1	**88.67**	11.07	0.26
		S8 horiz							39.45	99.3	**86.79**	12.95	0.26
		S9 horiz							38.34	99.2	**84.48**	15.26	0.25
		Avg							39.61	100.2	**86.20**	13.50	0.30
31m **rpt**	**31.8**	S5 horiz							39.31	98.9	**86.55**	13.21	0.24
		S6 horiz							39.18	98.6	**84.35**	15.34	0.31
		S7 horiz							40.16	101.1	**88.12**	11.23	0.65
		S8 horiz							40.72	102.5	**86.62**	13.13	0.26
		S9 horiz							37.64	100.1	**84.32**	15.40	0.28
		Avg							39.40	100.2	**85.99**	13.66	0.35
36	**36.0**	S1 horiz							39.932	100.5	**87.61**	11.87	0.52
		S2 horiz							40.572	102.1	**86.49**	12.74	0.77
		S3 horiz							41.397	104.2	**86.69**	12.77	0.54
		S4 down							39.462	99.3	**98.52**	1.31	0.17
		Avg							40.34	101.52	**89.83**	9.67	0.50

#4	t=0	**0.0**	S1	0	0	532	79812	0	0	41.81	100.0	**99.34**	0.66	0.00	
			S2	0	0	464	75433	0	0	39.44	100.0	**99.39**	0.61	0.00	
			S3	0	0	486	75338	0	0	39.40	100.0	**99.36**	0.64	0.00	
			S4	0	0	503	76975	0	0	40.28	100.0	**99.35**	0.65	0.00	
			Avg	0	0	496	76890	0	0	40.23	100.0	**99.36**	0.64	0.00	
	0.5	**0.5**	S1	0	0	565	80492	0	0	41.11	102.2	**99.30**	0.70	0.00	
			S2	0	0	577	78438	0	0	40.04	99.5	**99.27**	0.73	0.00	
			S3	0	0	554	78021	0	0	39.81	99.0	**99.29**	0.71	0.00	
			S4	0	0	554	78157	0	0	39.88	99.1	**99.30**	0.70	0.00	
			Avg	0	0	563	78777	0	0	40.21	100.0	**99.29**	0.71	0.00	
	1m	**1.0**	S1	0	0	522	78859	0	0	40.14	99.8	**99.34**	0.66	0.00	
			S2	0	0	544	78133	0	0	39.80	98.9	**99.31**	0.69	0.00	
			S3	0	0	495	77962	0	0	39.70	98.7	**99.37**	0.63	0.00	
			S4	0	0	483	77221	0	0	39.34	97.8	**99.38**	0.62	0.00	
			Avg	0	0	511	78044	0	0	39.75	98.8	**99.35**	0.65	0.00	
	2m	**2.1**	S1	0	0	716	76568	102	51	38.79	96.4	**98.88**	0.92	0.20	
			S2	0	0	604	75606	65	48	38.23	95.0	**99.06**	0.79	0.15	
			S3	0	0	615	78758	73	32	39.80	98.9	**99.09**	0.77	0.13	
			S4	0	0	592	76486	70	35	38.66	96.1	**99.10**	0.77	0.14	
			Avg	0	0	632	76855	78	42	38.87	96.6	**99.03**	0.81	0.15	
	3m	**3.0**	S1	0	45	732	83125	174	0	40.09	99.7	**98.87**	0.92	0.21	
			S2	0	92	736	83372	205	76	40.29	100.1	**98.69**	0.98	0.33	
			S3	0	44	716	81233	203	0	39.19	97.4	**98.83**	0.92	0.25	
			S4	0	114	801	84654	239	0	40.93	101.7	**98.66**	1.07	0.28	
			Avg	0	74	746	83096	205	19	40.12	99.7	**98.76**	0.97	0.27	
	4m	**3.9**	S1	0	0	711	82136	0	0	40.16	99.8	**99.14**	0.86	0.00	
			S1(rerun)	0	0	763	80847	21	0	41.12	102.2	**99.04**	0.93	0.03	re-injected ON
			S2	0	0	711	78787	0	0	38.53	95.8	**99.11**	0.89	0.00	
			S3	0	0	657	79751	0	0	38.98	96.9	**99.18**	0.82	0.00	
			S4	0	0	691	79247	0	0	38.75	96.3	**99.14**	0.86	0.00	
			Avg	0	0	707	80154	4	0	39.20	97.4	**99.12**	0.87	0.01	
	5m	**4.9**	S1	0	0	623	75691	104	0	39.93	99.2	**99.05**	0.82	0.14	
			S2	0	0	604	73742	96	0	38.91	96.7	**99.06**	0.81	0.13	
			S3	0	0	596	74711	193	0	39.45	98.1	**98.95**	0.79	0.26	
			S4	0	0	605	77284	0	0	40.69	101.1	**99.22**	0.78	0.00	
			Avg	0	0	607	75357	98	0	39.74	98.8	**99.07**	0.80	0.13	
	6m	**6.0**	S1	0	0	733	78903	84	0	40.71	101.2	**98.98**	0.92	0.11	
			S2	0	0	674	76708	78	0	39.52	98.2	**99.03**	0.87	0.10	
			S3	0	0	719	78125	86	0	40.30	100.2	**98.98**	0.91	0.11	
			S4	0	0	653	76033	119	0	39.17	97.4	**98.99**	0.85	0.15	
			Avg	0	0	695	77442	92	0	39.93	99.2	**98.99**	0.89	0.12	
	9m	**9.0**	S1	0	0	782	81978	57	0	39.71	98.7	**98.99**	0.94	0.07	
			S2	0	0	778	79138	134	0	38.34	95.3	**98.86**	0.97	0.17	
			S3	0	0	708	76946	0	0	37.16	92.4	**99.09**	0.91	0.00	
			S4	0	0	733	79815	0	0	38.59	95.9	**99.09**	0.91	0.00	
			Avg	0	0	750	79469	48	0	38.45	95.6	**99.01**	0.93	0.06	
	12m	**12.0**	S1	0	0	762	74929	101	0	38.97	96.9	**98.86**	1.01	0.13	
			S2	0	0	805	75494	109	0	39.29	97.7	**98.80**	1.05	0.14	
			S3	0	0	772	76150	107	0	39.62	98.5	**98.86**	1.00	0.14	
			S4	0	0	855	76473	116	0	39.84	99.0	**98.75**	1.10	0.15	
			Avg	0	0	799	75762	108	0	39.43	98.0	**98.82**	1.04	0.14	
	15m	**15.0**	S1	0	0	970	81420	1175	0	38.63	96.0	**97.43**	1.16	1.41	
			S2	0	0	912	80168	1044	0	37.96	94.4	**97.62**	1.11	1.27	
			S3	0	0	942	82905	0	0	38.76	96.3	**98.88**	1.12	0.00	
			S4	0	0	949	85560	0	0	39.99	99.4	**98.90**	1.10	0.00	
			Avg	0	0	943	82513	555	0	38.83	96.5	**98.22**	1.12	0.66	
	18m	**17.9**	S1	0	44	945	80940	128	84	41.06	102.1	**98.54**	1.20	0.26	
			S2	0	85	938	78741	148	98	39.98	99.4	**98.41**	1.28	0.31	
			S3	0	84	934	79869	154	180	40.59	100.9	**98.34**	1.25	0.41	
			S4	0	65	828	77484	108	56	39.24	97.5	**98.65**	1.14	0.21	
			Avg	0	70	911	79259	135	105	40.22	100.0	**98.49**	1.22	0.30	
	24m	**24.0**	S1	0	0	852093	73972867	6374	26231	41.15	102.3	**98.82**	1.14	0.04	
			S2	0	0	818073	72169498	20066	18993	40.14	99.8	**98.83**	1.12	0.05	
			S3	0	0	807431	71401736	17933	16832	39.71	98.7	**98.83**	1.12	0.05	
			S4	0	0	803845	72078799	16988	17381	40.08	99.6	**98.85**	1.10	0.05	
			Avg	0	0	820361	72405725	15340	19859	40.27	100.1	**98.83**	1.12	0.05	
	31m	**31.1**	S1 up							37.71	93.7	**98.46**	1.46	0.08	
			S2 up							39.21	97.5	**98.50**	1.39	0.11	
			S3 horiz							38.64	96.0	**76.74**	22.94	0.32	
			S4 down							39.39	97.9	**98.55**	1.37	0.08	
			Avg*							38.73	96.3	**98.50**	6.79	0.15	
	31m rpt	**31.1**	S3 horiz							40.01	99.5	**76.67**	22.90	0.43	
	32m	**31.8**	Horizontal 1							38.66	96.1	**77.85**	21.89	0.27	
			Horizontal 2							37.90	94.2	**85.11**	14.63	0.27	

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	36	**36.0**	S1							40.531	100.7	**98.32**	1.54	0.14	
			S2							40.678	101.1	**98.3**	1.44	0.27	
			S3							39.847	99.0	**98.29**	1.46	0.26	
			S4							40.572	100.8	**98.31**	1.4	0.29	
			Avg							40.41	100.4	**98.31**	1.5	0.24	
#5	t=0	**0.0**	S1	0	0	509	79339	0	0	41.55	100.0	**99.36**	0.64	0.00	
			S2	0	0	492	75410	0	0	39.44	100.0	**99.35**	0.65	0.00	
			S3	0	0	530	77056	0	0	40.34	100.0	**99.32**	0.68	0.00	
			S4	0	0	474	75743	0	0	39.61	100.0	**99.38**	0.62	0.00	
			Avg	0	0	501	76887	0	0	40.23	100.0	**99.35**	0.65	0.00	
	0.5	**0.5**	S1	0	0	572	80640	0	0	41.19	102.4	**99.30**	0.70	0.00	
			S2	0	0	523	76420	0	0	38.96	96.8	**99.32**	0.68	0.00	
			S3	0	0	535	77569	67	0	39.60	98.4	**99.23**	0.68	0.09	
			S4	0	0	538	75644	0	0	38.56	95.8	**99.29**	0.71	0.00	
			Avg	0	0	542	77568	17	0	39.58	98.4	**99.28**	0.69	0.02	
	1m	**1.0**	S1	0	0	514	79748	0	0	40.56	100.8	**99.36**	0.64	0.00	
			S2	0	0	498	78722	0	0	40.06	99.6	**99.37**	0.63	0.00	
			S3	0	0	510	79720	0	0	40.55	100.8	**99.36**	0.64	0.00	
			S4	0	0	504	78293	0	0	39.86	99.1	**99.36**	0.64	0.00	
			Avg	0	0	507	79121	0	0	40.26	100.1	**99.36**	0.64	0.00	
	2m	**2.1**	S1	0	0	579	76067	56	36	38.44	95.5	**99.13**	0.75	0.12	
			S2	0	0	690	75710	269	0	38.40	95.5	**98.75**	0.90	0.35	
			S3	0	0	571	75276	144	25	38.08	94.7	**99.03**	0.75	0.22	
			S4	0	0	613	76881	57	85	38.88	96.6	**99.03**	0.79	0.18	
			Avg	0	0	613	75984	132	37	38.45	95.6	**98.98**	0.80	0.22	
	3m	**3.0**	S1	0	11	734	85186	284	0	41.12	102.2	**98.81**	0.86	0.33	
			S2	0	94	718	79411	163	71	38.35	95.3	**98.70**	1.01	0.29	
			S3	0	54	699	81821	238	0	39.48	98.1	**98.80**	0.91	0.29	
			S4	0	96	796	83418	240	0	40.32	100.2	**98.66**	1.05	0.28	
			Avg	0	64	737	82459	231	18	39.82	99.0	**98.74**	0.96	0.30	
	4m	**3.9**	S1	0	344	745	82388	58	0	40.50	100.7	**98.63**	1.30	0.07	
			S1(re-inj)	0	362	769	79871	0	0	39.26	97.6	**98.60**	1.40	0.00	re-injected
			S2	0	0	654	80055	0	0	39.12	97.2	**99.19**	0.81	0.00	
			S3	0	0	660	77948	0	0	38.10	94.7	**99.16**	0.84	0.00	
			S4	0	0	670	77444	0	0	37.86	94.1	**99.14**	0.86	0.00	
			Avg	0	141	700	79541	12	0	38.97	96.9	**98.94**	1.05	0.01	
	5m	**4.9**	S1	0	0	633	75976	103	0	40.08	99.6	**99.04**	0.83	0.13	
			S2	0	0	576	76082	209	0	40.16	99.8	**98.98**	0.75	0.27	
			S3	0	0	581	74519	0	0	39.25	97.6	**99.23**	0.77	0.00	
			S4	0	0	562	74028	58	0	39.01	97.0	**99.17**	0.75	0.08	
			Avg	0	0	588	75151	93	0	39.63	98.5	**99.10**	0.78	0.12	
	6m	**6.0**	S1	0	0	748	77213	95	0	39.83	99.0	**98.92**	0.96	0.12	
			S2	0	0	657	75129	83	0	38.68	96.1	**99.02**	0.87	0.11	
			S3	0	0	682	76991	72	0	39.67	98.6	**99.03**	0.88	0.09	
			S4	0	0	662	75721	91	0	39.00	96.9	**99.02**	0.87	0.12	
			Avg	0	0	687	76264	85	0	39.30	97.7	**99.00**	0.89	0.11	
	9m	**9.0**	S1	0	0	808	82195	0	0	39.80	98.9	**99.03**	0.97	0.00	
			S2	0	0	724	78070	0	0	37.72	93.8	**99.08**	0.92	0.00	
			S3	0	0	748	77773	0	0	37.59	93.4	**99.05**	0.95	0.00	
			S4	0	0	747	78913	0	0	38.15	94.8	**99.06**	0.94	0.00	
			Avg	0	0	757	79238	0	0	38.31	95.2	**99.05**	0.95	0.00	
	12m	**12.0**	S1	0	0	869	75816	105	0	39.49	98.2	**98.73**	1.13	0.14	
			S2	0	0	761	74091	52	0	38.49	95.7	**98.91**	1.02	0.07	
			S3	0	0	803	75058	118	0	39.06	97.1	**98.79**	1.06	0.16	
			S4	0	0	771	72470	67	0	37.65	93.6	**98.86**	1.05	0.09	
			Avg	0	0	801	74359	86	0	38.68	96.1	**98.82**	1.06	0.11	
	15m	**15.0**	S1	0	0	920	80780	1155	0	38.30	95.2	**97.50**	1.11	1.39	
			S2	0	0	955	83997	1193	0	39.82	99.0	**97.51**	1.11	1.38	
			S3	0	0	895	82020	0	0	38.33	95.3	**98.92**	1.08	0.00	
			S4	0	0	948	84106	0	0	39.32	97.7	**98.89**	1.11	0.00	
			Avg	0	0	930	82726	587	0	38.94	96.8	**98.20**	1.10	0.70	
	18m	**17.9**	S1	0	64	952	79618	145	70	40.41	100.4	**98.48**	1.26	0.27	
			S2	0	97	937	79040	132	67	40.12	99.7	**98.46**	1.29	0.25	
			S3	0	135	923	78493	146	104	39.88	99.1	**98.36**	1.33	0.31	
			S4	0	0	1001	78823	156	104	40.02	99.5	**98.43**	1.25	0.32	
			Avg	0	74	953	78994	145	86	40.10	99.7	**98.43**	1.28	0.29	
	24m	**24.0**	S1	0	0	864455	75078288	17157	21619	41.76	103.8	**98.81**	1.14	0.05	
			S2	0	0	817414	71416790	17068	19174	39.73	98.7	**98.82**	1.13	0.05	
			S3	0	0	829923	71881431	17362	19717	39.99	99.4	**98.81**	1.14	0.05	
			S4	0	0	900761	74301871	15033	21442	41.36	102.8	**98.75**	1.20	0.05	
			Avg	0	0	853138	73169595	16655	20488	40.71	101.2	**98.80**	1.15	0.05	
	31m	**31.1**	S1 up							39.03	97.0	**98.50**	1.42	0.08	
			S2 up							37.33	92.8	**98.51**	1.40	0.09	
			S3 horiz							38.54	95.8	**67.69**	32.04	0.28	
			S4 down							38.75	96.3	**98.46**	1.41	0.13	
			Avg*							38.41	95.5	**98.49**	9.07	0.15	
	31m rpt	**31.1**	S3 horiz							37.95	94.3	**67.74**	31.99	0.28	
	32m	**31.8**	Horizontal 1							42.05	104.5	**67.27**	32.39	0.34	
			Horizontal 2							38.27	95.1	**66.59**	33.08	0.33	
	36	**36.0**	S1							41.561	103.3	**98.34**	1.43	0.22	
			S2							40.001	99.4	**98.44**	1.37	0.19	
			S3							39.861	99.1	**98.51**	1.37	0.12	
			S4							40.43	100.5	**98.41**	1.42	0.18	
			Avg							40.46	100.57	**98.43**	1.40	0.18	

#6	t=0	**0.0**	S1	0	0	598	80845	0	0	42.40	100.0	**99.27**	0.73	0.00	
			S2	0	0	510	74541	0	0	38.98	100.0	**99.32**	0.68	0.00	
			S3	0	0	549	74683	0	0	39.08	100.0	**99.27**	0.73	0.00	
			S4	0	0	497	75679	0	0	39.58	100.0	**99.35**	0.65	0.00	
			Avg	0	0	539	76437	0	0	40.01	100.0	**99.30**	0.70	0.00	
	0.5	**0.5**	S1	0	0	620	79838	55	0	40.83	102.0	**99.16**	0.77	0.07	
			S2	0	0	576	77503	0	0	39.55	98.9	**99.26**	0.74	0.00	
			S3	0	0	575	77020	43	0	39.32	98.3	**99.20**	0.74	0.06	
			S4	0	0	566	78424	61	0	40.06	100.1	**99.21**	0.72	0.08	
			Avg	0	0	584	78196	40	0	39.94	99.8	**99.21**	0.74	0.05	
	1m	**1.0**	S1	0	0	532	79709	0	0	40.55	101.4	**99.34**	0.66	0.00	
			S2	0	0	503	76965	0	0	39.22	98.0	**99.35**	0.65	0.00	
			S3	0	0	523	78239	0	0	39.84	99.6	**99.34**	0.66	0.00	
			S4	0	0	543	78152	0	0	39.81	99.5	**99.31**	0.69	0.00	
			Avg	0	0	525	78266	0	0	39.86	99.6	**99.33**	0.67	0.00	
	2m	**2.1**	S1	0	0	618	78153	47	22	39.48	98.7	**99.13**	0.78	0.09	
			S2	0	0	635	76089	93	89	38.52	96.3	**98.94**	0.83	0.24	
			S3	0	0	613	76575	85	63	38.74	96.8	**99.02**	0.79	0.19	
			S4	0	0	617	75396	53	40	38.12	95.3	**99.07**	0.81	0.12	
			Avg	0	0	621	76553	70	54	38.72	96.8	**99.04**	0.80	0.16	
	3m	**3.0**	S1	0	114	796	85692	290	0	41.45	103.6	**98.62**	1.05	0.33	
			S2	0	126	646	83541	205	63	40.34	100.8	**98.77**	0.91	0.32	
			S3	0	78	728	84490	195	0	40.77	101.9	**98.83**	0.94	0.23	
			S4	0	62	771	83146	270	0	40.18	100.4	**98.69**	0.99	0.32	
			Avg	0	95	735	84217	240	16	40.68	101.7	**98.73**	0.97	0.30	
	4m	**3.9**	S1	0	105	782	81636	0	0	40.00	100.0	**98.93**	1.07	0.00	
			S2	0	0	718	80957	0	0	39.59	98.9	**99.12**	0.88	0.00	
			S3	0	0	700	78864	0	0	38.56	96.4	**99.12**	0.88	0.00	
			S4	0	0	680	80667	0	0	39.43	98.6	**99.16**	0.84	0.00	
			S1(re-inj)	0	118	841	79620	0	0	39.06	97.6	**98.81**	1.19	0.00	re-injected
			Avg	0	26	720	80531	0	0	39.40	98.5	**99.08**	0.92	0.00	
	5m	**4.9**	S1	0	0	607	75187	0	0	39.61	99.0	**99.20**	0.80	0.00	
			S2	0	0	610	75004	144	0	39.59	98.9	**99.00**	0.81	0.19	
			S3	0	0	631	74901	0	0	39.47	98.6	**99.16**	0.84	0.00	
			S4	0	0	609	74375	0	0	39.19	97.9	**99.19**	0.81	0.00	
			Avg	0	0	614	74867	36	0	39.46	98.6	**99.14**	0.81	0.05	
	6m	**6.0**	S1	0	0	711	77687	111	0	40.07	100.2	**99.09**	0.88	0.03	
			S2	0	0	681	75582	98	0	38.94	97.3	**99.09**	0.88	0.03	
			S3	0	0	644	75226	90	0	38.73	96.8	**99.12**	0.84	0.04	
			S4	0	0	704	77959	79	0	40.20	100.5	**99.10**	0.87	0.03	
			Avg	0	0	685	76614	95	0	39.48	98.7	**99.10**	0.87	0.03	
	9m	**9.0**	S1	0	0	914	86511	88	89	42.07	105.1	**98.75**	1.04	0.20	
			S2	0	0	758	79663	0	0	38.52	96.3	**99.06**	0.94	0.00	
			S3	0	0	758	79482	0	0	38.44	96.1	**99.06**	0.94	0.00	
			S4	0	0	776	81508	113	0	39.50	98.7	**98.92**	0.94	0.14	
			Avg	0	0	802	81791	50	22	39.63	99.0	**98.95**	0.97	0.08	
	12m	**12.0**	S1	0	0	871	74457	73	0	38.76	96.9	**98.75**	1.16	0.10	
			S2	0	0	769	72588	89	0	37.72	94.3	**98.83**	1.05	0.12	
			S3	0	0	792	73128	66	0	38.01	95.0	**98.84**	1.07	0.09	
			S4	0	0	757	72737	60	0	37.78	94.4	**98.89**	1.03	0.08	
			Avg	0	0	797	73228	72	0	38.07	95.1	**98.83**	1.08	0.10	
	15m	**15.0**	S1	0	0	914	81409	0	0	38.05	95.1	**98.89**	1.11	0.00	
			S2	0	0	947	82616	0	0	38.63	96.5	**98.87**	1.13	0.00	
			S3	0	0	951	85492	0	0	39.96	99.9	**98.90**	1.10	0.00	
			S4	0	0	878	82709	0	0	38.64	96.6	**98.95**	1.05	0.00	
			Avg	0	0	923	83057	0	0	38.82	97.0	**98.90**	1.10	0.00	
	18m	**17.9**	S1	0	0	980	78981	113	96	40.06	100.1	**98.52**	1.22	0.26	
			S2	0	0	903	78465	122	76	39.76	99.4	**98.62**	1.13	0.25	
			S3	0	0	971	79439	116	86	40.29	100.7	**98.54**	1.20	0.25	
			S4	0	0	950	80390	115	50	40.74	101.8	**98.63**	1.17	0.20	
			Avg	0	0	951	79319	117	77	40.21	100.5	**98.58**	1.18	0.24	
	24m	**24.0**	S1	0	0	850591	74394963	15915	22765	41.38	103.4	**98.82**	1.13	0.05	
			S2	0	0	846730	73566898	8580	20959	40.92	102.3	**98.81**	1.14	0.05	
			S3	0	0	834284	72913931	12506	26876	40.56	101.4	**98.82**	1.13	0.05	
			S4	0	0	847303	72795280	18070	21280	40.50	101.2	**98.80**	1.15	0.05	
			Avg	0	0	844727	73417768	13768	22970	40.84	102.1	**98.81**	1.14	0.05	
	31m	**31.1**	S1 up							38.45	96.1	**98.53**	1.39	0.08	
			S2 up							37.26	93.1	**98.53**	1.39	0.08	
			S3 horiz							39.92	99.8	**90.94**	8.80	0.26	
			S4 down							39.79	99.4	**98.56**	1.34	0.10	
			Avg*							38.85	97.1	**98.54**	3.23	0.13	
	31m rpt	**31.1**	S3 horiz							38.21	95.5	**90.97**	8.76	0.27	
	32m	**31.8**	Horizontal 1							39.50	98.7	**92.63**	7.10	0.27	
			Horizontal 2							40.89	102.2	**92.43**	7.29	0.27	
	36	**36.0**	S1							40.103	100.2	**98.53**	1.38	0.09	
			S2							39.937	99.8	**98.37**	1.46	0.17	
			S3							39.676	99.2	**98.17**	1.41	0.42	
			S4							40.858	102.1	**98.44**	1.35	0.21	
			Avg							40.14	100.3	**98.38**	1.4	0.22	

#7	t=0	**0.0**	S1	0	0	412	77578	0	0	40.55	100.0	**99.47**	0.53	0.00	
			S2	0	0	376	76712	0	0	40.07	100.0	**99.51**	0.49	0.00	
			Ave	0	0	394	77145	0	0	40.31	100.0	**99.49**	0.51	0.00	
	0.5m	**0.5**	S1	0	0	466	78337	0	0	39.93	99.1	**99.41**	0.59	0.00	
			S2	0	0	455	78333	0	0	39.92	99.0	**99.42**	0.58	0.00	
			Ave	0	0	461	78335	0	0	39.93	99.0	**99.42**	0.58	0.00	
	1m	**1.0**	S1	0	0	402	78138	0	0	39.74	98.6	**99.49**	0.51	0.00	
			S2	0	0	402	77183	0	0	39.28	97.4	**99.48**	0.52	0.00	
			Ave	0	0	402	77661	0	0	39.51	98.0	**99.49**	0.51	0.00	
	2m	**2.1**	S1	0	0	506	75880	55	44	38.31	95.0	**99.21**	0.66	0.13	
			S2	0	0	531	75619	119	0	38.21	94.8	**99.15**	0.70	0.16	
			Ave	0	0	519	75750	87	22	38.26	94.9	**99.18**	0.68	0.14	
	3m	**3.0**	S1	0	105	643	85678	320	0	41.38	102.6	**98.77**	0.86	0.37	
			S2	0	98	744	81295	203	50	39.28	97.4	**98.67**	1.02	0.31	
			S3	0	80	593	82530	56	0	39.70	98.5	**99.12**	0.81	0.07	
			Ave	0	94	660	83168	193	17	40.12	99.5	**98.85**	0.90	0.25	
	4m	**3.9**	S1	0	2239	663	81981	0	0	41.15	102.1	**96.58**	3.42	0.00	
			S1(re-inj)	63	2250	720	82687	32	0	41.57	103.1	**96.43**	3.54	0.04	
			S1(re-inj)	59	2187	754	81015	0	0	40.73	101.0	**96.43**	3.57	0.00	re-injected
			S2	0	0	600	79682	0	0	38.91	96.5	**99.25**	0.75	0.00	
			Ave	31	1669	684	81341	8	0	40.59	100.7	**97.17**	2.82	0.01	
	5m	**4.9**	S1	0	0	619	76580	0	0	40.33	100.0	**99.20**	0.80	0.00	
			S2	0	0	576	74456	100	0	39.26	97.4	**99.10**	0.77	0.13	
			Ave	0	0	598	75518	50	0	39.80	98.7	**99.15**	0.78	0.07	
	6m	**6.0**	S1	0	0	663	79739	82	0	41.12	102.0	**99.07**	0.82	0.10	
			S2	0	0	607	77887	89	0	40.11	99.5	**99.11**	0.77	0.11	
			S3	0	0	608	76721	107	0	39.51	98.0	**99.08**	0.79	0.14	
			Ave	0	0	626	78116	93	0	40.25	100.7	**99.09**	0.80	0.11	
	9m	**9.0**	S1	0	0	742	83727	88	0	40.56	100.6	**99.02**	0.88	0.10	
			S2	0	0	634	79804	113	0	38.59	95.7	**99.07**	0.79	0.14	
			S3	0	0	645	80733	0	0	39.00	96.7	**99.21**	0.79	0.00	
			Ave	0	0	674	81421	67	0	39.38	97.7	**99.10**	0.82	0.08	
	12m	**12.0**	S1	0	0	730	76696	71	0	39.87	98.9	**98.97**	0.94	0.09	
			S2	0	0	669	73390	58	0	38.08	94.5	**99.02**	0.90	0.08	
			avg	0	0	700	75043	65	0	38.97	96.7	**98.99**	0.92	0.09	
	15m	**15.0**	S1	0	38	718	77313	0	0	36.62	90.8	**99.03**	0.97	0.00	
			S2	0	43	752	79290	235	54	37.73	93.6	**98.65**	0.99	0.36	
			Avg	0	41	735	78302	118	27	37.17	92.2	**98.84**	0.98	0.18	
	18m	**17.9**	S1	0	70	844	77690	120	124	39.39	97.7	**98.53**	1.16	0.31	
	24m	**24.0**	S1	0	0	668553	65459306	16102	21952	39.74	98.6	**98.92**	1.03	0.06	
	31.4	**31.6**	S1							39.05	96.9	**98.58**	1.34	0.08	
	31.4 **rpt**	**31.6**	S1							38.75	96.1	**98.48**	1.35	0.18	
	36m	**36.0**	S1							40.403	100.2	**98.66**	1.2	0.14	

t=0 seq 060117F
t=0.5m, seq 060128G
t=1m, seq 060214G
t=2m, seq 060320F

t=4m, seq 060524H (reinjected samples on 060523F)
t=5m seq 060613GA
t=6m seq 060720B

t=3m seq 060607F (D1-3)
t=3m seq 060613E (D4-7, and D2S2, D3S2)
t=4m D4S1 seq 0607C07B (re-inj)
t=1m D2S4 seq 0607C07B (re-inj)
t=2m D2S4 seq 0607C07B (re-inj)
t=9m D1-D7 Seq 061016K
t=12m D1-D7 Seq 070115B
t=15m D1-2, 7 seq 070417E
t= 15m D3-6 Seq 070416K

18m D3,D7 seq 070716E m= 3954.2 b= 961.03 inj vol= 0.5 %RSD=0.1 **std 10mg/ml EF-4630-13**

Sequence	SE-HPLC C-ISO method		working STD lot	working STD conc	slope	int	injection volume (uL)	Corr Coef	% STD deviation	Sample IDs	Cal ID	Cal Curve ID
Empower 080118Max	NA		EF-7630-13	10mg/mL	**3.65E+00**	**-1.71E+00**	**0.5**	0.9996	0.60	24m D1-D7	4676.00	
080821 Pam	NA		EF-7630-13	10mg/mL	**3.96E+06**	**1.28E+06**	**0.5**	0.9996	1.80	31m D1-D7	16754.00	
080827 Pam	NA		EF-7630-13	10mg/mL	3.93E+06	-3.77E+05	0.5	0.9997		D3 S1 - S5 horiz 31m	17273.00	17275
080905 Pam	NA		EF-7630-13	10mg/mL	3.94E+06	7.17E+05	1.0	0.9995	0.80	**31m** (**Repeat** horizontal syr for D1,D2,D4,D5,D6), **32m** (2x horizontal), (D7 31.4m rpt)	17774.00	17776
* 31m AVG is the average excluding the horizontal outliers												
090116 Pam	NA		EF-7630-13	10mg/mL	**3.90E+06**	**5.28E+05**	**0.5**	0.9992	1.2	36m D3 D6	21680	NA

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Device	Length of stress (months) Theoretical	Length of stress (months) Actual	Syringe	HMW Peak Area	HMW Peak Area	HMW Peak Area	Native Peak Area	LMW Peak Area	LMW Peak Area	[VEGF-TRAP] mg/ml	% VEGF-TRAP Recov-ered	% Native VEGF-TRAP	% HMW Species	% LMW Species	
#1	t=0	0.0	S1	0	0	549	80482	0	0	42.2	100.0	99.3	0.7	0.0	
			S2	0	0	497	73534	0	0	38.4	100.0	99.3	0.7	0.0	
			S3	0	0	499	76050	0	0	39.8	100.0	99.3	0.7	0.0	
			S4	0	0	490	75245	0	0	39.3	100.0	99.4	0.6	0.0	
			Avg	0	0	509	76328	0	0	39.9	100.0	99.3	0.7	0.0	
	0.5	0.5	S1	0	0	778	81294	100	44	41.7	104.5	98.9	0.9	0.2	
			S2	0	0	695	76645	105	76	39.3	98.3	98.9	0.9	0.2	
			S3	0	0	730	77741	114	68	39.9	99.8	98.8	0.9	0.2	
			S4	0	0	701	76439	122	67	39.2	98.1	98.8	0.9	0.2	
			Avg	0	0	726	78030	110	64	40.0	100.2	98.9	0.9	0.2	
	1m	1.0	S1	0	0	761	76966	354	290	39.7	99.3	98.2	1.0	0.8	
			S2	0	0	827	77250	357	273	39.8	99.7	98.1	1.1	0.8	
			S3	0	0	830	78871	322	333	40.6	101.7	98.2	1.0	0.8	
			S4	0	0	797	79022	342	285	40.7	101.8	98.2	1.0	0.8	
			Avg	0	0	804	78027	344	295	40.2	100.6	98.2	1.0	0.8	
	2m	2.1	S1	0	56	1141	79261	151	218	39.7	99.4	98.1	1.5	0.5	
			S2	0	27	1190	80552	227	177	40.4	101.0	98.0	1.5	0.5	
			S3	0	52	1093	77770	174	248	38.9	97.5	98.0	1.4	0.5	
			S4	0	59	1069	79096	195	266	39.6	99.2	98.0	1.4	0.6	
			Avg	0	49	1123	79170	187	227	39.6	99.3	98.0	1.5	0.5	
	3m	3.0	S1	0	40	1098	79310	430	382	45.1	112.9	97.6	1.4	1.0	
			S2	0	30	906	67757	353	275	38.9	97.5	97.7	1.4	0.9	
			S3	0	22	1061	74688	385	309	42.6	106.7	97.7	1.4	0.9	
			S4	0	49	1302	80092	228	224	39.2	98.1	97.8	1.6	0.6	(re-run on
			Avg	0	35	1092	75462	349	298	43.0	107.7	97.7	1.5	0.8	
	4m	3.9	S1	0	75	1428	80996	263	289	40.3	100.8	97.5	1.8	0.7	
			S2	0	39	1345	78724	252	249	39.1	97.8	97.7	1.7	0.6	
			S3	0	63	1391	77893	248	262	38.7	96.9	97.5	1.8	0.6	
			S4	0	49	1419	79890	263	256	39.7	99.4	97.6	1.8	0.6	
			Avg	0	57	1396	79376	257	264	39.4	98.7	97.6	1.8	0.6	
	5m	4.9	S1	0	48	1309	75677	394	380	40.6	101.8	97.3	1.7	1.0	
			S2	0	54	1317	72987	452	410	39.3	98.4	97.0	1.8	1.1	
			S3	0	60	1263	72568	426	347	39.0	97.7	97.2	1.8	1.0	
			S4	0	42	1190	73043	391	324	39.2	98.1	97.4	1.6	1.0	
			Avg	0	51	1270	73569	416	365	39.5	99.0	97.2	1.7	1.0	
	6m	6.0	S1	0	53	1405	75305	477	439	39.6	99.2	96.9	1.9	1.2	
			S2	0	41	1328	73632	449	386	38.7	96.8	97.1	1.8	1.1	
			S3	0	61	1454	77429	460	419	40.8	102.1	97.0	1.9	1.1	
			S4	0	45	1306	73797	434	411	38.7	97.0	97.1	1.8	1.1	
			Avg	0	50	1373	75041	455	414	39.5	98.8	97.0	1.8	1.1	
	31m	31.3	S1							40.674	101.8	86.12	11.22	2.66	
			S2							41.769	104.6	85.55	11.5	2.96	

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			S3				43.964	110.1	85.65	11.54	2.81
			S4				41.619	104.2	86.53	10.75	2.72
			Avg				42.0	105.2	86.0	11.3	2.8

#2	t=0	0.0	S1	0	0	527	78972	0	0	41.4	100.0	99.3	0.7	0.0
			S2	0	0	478	74712	0	0	39.1	100.0	99.4	0.6	0.0
			S3	0	0	479	76710	0	0	40.1	100.0	99.4	0.6	0.0
			S4	0	0	478	76037	0	0	39.8	100.0	99.4	0.6	0.0
			Avg	0	0	491	76608	0	0	40.1	100.0	99.4	0.6	0.0
	0.5	0.5	S1	0	0	733	80421	149	67	41.3	103.0	98.8	0.9	0.3
			S2	0	0	703	76911	118	82	39.4	98.3	98.8	0.9	0.3
			S3	0	0	706	78878	105	69	40.4	100.9	98.9	0.9	0.2
			S4	0	0	694	77026	136	78	39.5	98.5	98.8	0.9	0.3
			Avg	0	0	709	78309	127	74	40.1	100.2	98.9	0.9	0.3
	1m	1.0	S1	0	0	779	76817	340	289	39.6	98.8	98.2	1.0	0.8
			S2	0	0	749	77432	319	257	39.8	99.4	98.3	1.0	0.7
			S3	0	0	816	80629	326	300	41.4	103.4	98.2	1.0	0.8
			S4	0	0	782	76519	335	296	39.4	98.4	98.2	1.0	0.8
			Avg	0	0	782	77849	330	286	40.1	100.0	98.2	1.0	0.8
	2m	2.1	S1	0	37	1025	80547	166	126	40.2	100.3	98.3	1.3	0.4
			S2	0	33	1011	79900	143	48	39.8	99.4	98.5	1.3	0.2
			S3	0	51	1018	79776	137	52	39.8	99.3	98.4	1.3	0.2
			S4	0	39	1061	79058	196	240	39.6	98.7	98.1	1.4	0.5
			Avg	0	40	1029	79820	161	117	39.8	99.4	98.3	1.3	0.3
	3m	3.0	S1	0	22	809	61051	321	272	35.4	88.3	97.7	1.3	0.9
			S2	0	24	1040	77361	369	321	44.0	109.8	97.8	1.3	0.9
			S3	0	20	1027	78373	336	227	44.4	110.9	98.0	1.3	0.7
			S4	0	34	1122	78011	359	330	44.4	110.7	97.7	1.4	0.9
			Avg	0	25	1000	73699	346	288	42.0	104.9	97.8	1.4	0.8
	4m	3.9	S1	0	45	1416	81973	293	318	40.7	101.7	97.5	1.7	0.7
			S2	0	50	1302	78717	232	220	39.0	97.4	97.8	1.7	0.6
			S3	0	44	1288	77039	221	206	38.2	95.3	97.8	1.7	0.5
			S4	0	62	1383	78519	263	236	39.0	97.3	97.6	1.8	0.6
			Avg	0	50	1347	79062	252	245	39.2	97.9	97.7	1.7	0.6
	5m	4.9	S1	0	53	1281	73945	412	359	39.7	99.2	97.2	1.8	1.0
			S2	0	62	1249	73422	434	386	39.5	98.5	97.2	1.7	1.1
			S3	0	53	1244	73185	413	352	39.3	98.1	97.3	1.7	1.0
			S4	0	44	1298	73547	392	311	39.5	98.6	97.3	1.8	0.9
			Avg	0	53	1268	73525	413	352	39.5	98.6	97.2	1.7	1.0
	6m	6.0	S1	0	49	1376	75372	458	419	39.6	98.9	97.0	1.8	1.1
			S2	0	44	1405	76377	447	384	40.2	100.2	97.1	1.8	1.1
			S3	0	50	1400	76501	463	416	40.2	100.4	97.0	1.8	1.1
			S4	0	59	1433	77343	454	424	40.7	101.6	97.0	1.9	1.1
			Avg	0	51	1404	76398	456	411	40.2	100.3	97.1	1.8	1.1
	31m	31.3	S1							41.311	103.1	85.7	11.5	2.8
			S2							39.031	97.4	85.79	11.51	2.7
			S3							39.067	97.5	86.0	11.19	2.82
			S4							38.785	96.8	85.1	12.21	2.69
			Avg							39.5	98.7	85.6	11.6	2.8

#3	t=0	0.0	S1	0	0	498	78967	0	0	41.3	100.0	99.4	0.6	0.0
			S2	0	0	451	74099	0	0	38.7	100.0	99.4	0.6	0.0
			S3	0	0	472	75574	0	0	39.5	100.0	99.4	0.6	0.0
			S4	0	0	482	75293	0	0	39.4	100.0	99.4	0.6	0.0
			Avg	0	0	476	75983	0	0	39.7	100.0	99.4	0.6	0.0
	0.5	0.5	S1	0	0	757	79965	123	60	41.0	103.3	98.8	0.9	0.2
			S2	0	0	686	76676	127	99	39.3	98.9	98.8	0.9	0.3
			S3	0	0	745	78720	158	111	40.4	101.7	98.7	0.9	0.3
			S4	0	0	637	77304	115	70	39.6	99.6	98.9	0.8	0.2
			Avg	0	0	706	78166	131	85	40.1	100.9	98.8	0.9	0.3
	1m	1.0	S1	0	0	752	76731	355	265	39.5	99.5	98.2	1.0	0.8
			S2	0	0	749	79014	318	294	40.6	102.2	98.3	0.9	0.8
			S3	0	0	747	78899	290	284	40.5	102.0	98.4	0.9	0.7
			S4	0	0	720	76448	291	271	39.3	99.0	98.4	0.9	0.7
			Avg	0	0	742	77773	314	279	40.0	100.7	98.3	0.9	0.7
	2m	2.1	S1	0	32	1008	80105	107	110	39.9	100.5	98.5	1.3	0.3
			S2	37	106	1050	79337	191	260	39.8	100.1	98.0	1.5	0.6
			S3	0	63	1022	77825	223	277	39.0	98.1	98.0	1.4	0.6
			S4	19	31	1011	79007	191	179	39.5	99.4	98.2	1.3	0.5
			Avg	14	58	1023	79069	178	207	39.5	99.5	98.2	1.4	0.5
	3m	3.0	S1	0	26	807	60774	335	341	35.3	88.8	97.6	1.3	1.1
			S2	0	20	1008	77734	340	269	44.1	111.1	97.9	1.3	0.8
			S3	0	20	875	66508	306	243	38.2	96.2	97.9	1.3	0.8
			S4	0	21	888	69161	307	225	39.6	99.6	98.0	1.3	0.8
			Avg	0	22	895	68544	322	270	39.3	98.9	97.8	1.3	0.8
	4m	3.9	S1	0	44	1339	81235	261	232	40.3	101.4	97.7	1.7	0.6
			S2	0	46	1274	77878	280	303	38.7	97.3	97.6	1.7	0.7
			S3	0	50	1280	78755	256	223	39.1	98.3	97.8	1.7	0.6
			S4	0	62	1287	77591	276	299	38.5	97.0	97.6	1.7	0.7
			Avg	0	51	1295	78865	268	264	39.1	98.5	97.7	1.7	0.7
	5m	4.9	S1	0	63	1264	75376	435	401	40.5	101.9	97.2	1.7	1.1
			S2	0	72	1280	75456	423	385	40.5	102.0	97.2	1.7	1.0
			S3	0	71	1282	74562	429	386	40.1	100.9	97.2	1.8	1.1
			S4	0	57	1294	76131	441	389	40.9	102.9	97.2	1.7	1.1
			Avg	0	66	1280	75381	432	390	40.5	102.0	97.2	1.7	1.1
	6m	6.0	S1	0	39	1311	74962	423	363	39.3	99.0	97.2	1.8	1.0
			S2	0	47	1410	77539	463	448	40.8	102.7	97.0	1.8	1.1
			S3	0	49	1364	75016	423	404	39.4	99.2	97.1	1.8	1.1
			S4	0	41	1301	75327	402	354	39.5	99.4	97.3	1.7	1.0
			Avg	0	44	1347	75711	428	392	39.8	100.1	97.2	1.8	1.1
	31m	31.3	S1							41.395	104.2	85.69	11.58	2.73
			S2							39.712	99.9	85.72	11.51	2.78
			S3							41.049	103.3	85.33	11.88	2.79
			S4							42.064	105.9	86.07	11.21	2.72
			Avg							41.1	103.3	85.7	11.5	2.8

#4	t=0	0.0	S1	0	0	532	79812	0	0	41.8	100.0	99.3	0.7	0.0	
			S2	0	0	464	75433	0	0	39.4	100.0	99.4	0.6	0.0	
			S3	0	0	486	75338	0	0	39.4	100.0	99.4	0.6	0.0	
			S4	0	0	503	76975	0	0	40.3	100.0	99.4	0.6	0.0	
			Avg	0	0	496	76890	0	0	40.2	100.0	99.4	0.6	0.0	
	0.5	0.5	S1	0	0	744	80263	110	40	41.2	102.3	98.9	0.9	0.2	
			S2	0	0	654	76745	105	66	39.3	97.7	98.9	0.8	0.2	
			S3	0	0	655	77379	93	47	39.6	98.4	99.0	0.8	0.2	
			S4	0	0	692	76500	144	97	39.2	97.5	98.8	0.9	0.3	
			Avg	0	0	686	77722	113	63	39.8	99.0	98.9	0.9	0.2	
	1m	1.0	S1	0	0	761	77968	307	252	40.1	99.7	98.3	1.0	0.7	
			S2	0	0	751	77392	351	244	39.8	99.0	98.3	1.0	0.8	
			S3	0	0	743	76619	333	259	39.5	98.1	98.3	1.0	0.8	
			S4	0	0	788	77485	334	267	39.9	99.2	98.2	1.0	0.8	
			Avg	0	0	761	77366	331	256	39.8	99.0	98.3	1.0	0.7	
	2m	2.1	S1	0	45	1161	83647	167	165	41.9	104.0	98.2	1.4	0.4	
			S2	0	82	1084	82605	172	215	41.3	102.8	98.2	1.4	0.5	
			S3	0	29	1037	80549	147	219	40.3	100.1	98.3	1.3	0.4	
			S4	0	41	1106	79283	186	163	39.7	98.6	98.1	1.4	0.4	
			Avg	0	49	1097	81521	168	191	40.8	101.4	98.2	1.4	0.4	
	3m	3.0	S1	0	30	1051	75923	308	212	43.2	107.3	97.9	1.4	0.7	
			S2	0	24	1012	75960	324	264	43.2	107.4	97.9	1.3	0.8	
			S3	0	20	939	69870	269	187	39.9	99.3	98.0	1.3	0.6	
			S4	0	29	1105	76508	288	204	43.5	108.1	97.9	1.5	0.6	
			Avg	0	26	1027	74565	297	217	42.4	105.5	97.9	1.4	0.7	
	4m	3.9	S1	0	53	1462	83117	241	237	40.7	101.2	97.7	1.8	0.6	(re-run on s
			S2	0	43	1350	76708	259	216	38.1	94.7	97.6	1.8	0.6	
			S3	0	49	1328	78348	260	250	38.9	96.7	97.6	1.7	0.6	
			S4	0	47	1365	78601	268	278	39.0	97.1	97.6	1.8	0.7	
			Avg	0	48	1376	79194	257	245	39.3	97.7	97.6	1.8	0.6	
	5m	4.9	S1	0	55	1337	76156	430	372	40.9	101.7	97.2	1.8	1.0	
			S2	0	70	1531	80107	290	282	39.4	97.8	97.4	1.9	0.7	(re-run on s
			S3	0	72	1227	73443	459	438	39.5	98.2	97.1	1.7	1.2	
			S4	0	66	1285	74405	479	421	40.1	99.6	97.1	1.8	1.2	
			Avg	0	66	1345	76028	415	378	40.0	99.3	97.2	1.8	1.0	
	6m	6.0	S1	0	65	1482	77766	435	414	40.9	101.8	97.0	1.9	1.1	
			S2	0	62	1431	73970	411	403	38.9	96.7	97.0	2.0	1.1	
			S3	0	56	1435	76661	413	412	40.3	100.2	97.1	1.9	1.0	
			S4	0	70	1535	75597	435	415	39.8	99.0	96.9	2.1	1.1	
			Avg	0	63	1471	75999	424	411	40.0	99.4	97.0	2.0	1.1	
	31m	31.3	S1							43.103	107.1	83.89	13.34	2.77	
			S2							39.023	97.0	83.34	13.82	2.84	
			S3							40.416	100.5	84.09	13.04	2.87	
			S4							41.966	104.3	83.42	13.72	2.86	
			Avg							41.1	102.2	83.7	13.5	2.8	

#5	t=0	0.0	S1	0	0	509	79339	0	0	41.5	100.0	99.4	0.6	0.0
			S2	0	0	492	75410	0	0	39.4	100.0	99.4	0.6	0.0
			S3	0	0	530	77056	0	0	40.3	100.0	99.3	0.7	0.0
			S4	0	0	474	75743	0	0	39.6	100.0	99.4	0.6	0.0
			Avg	0	0	501	76887	0	0	40.2	100.0	99.4	0.6	0.0
	0.5	0.5	S1	0	0	697	80604	0	0	41.2	102.5	99.1	0.9	0.0
			S2	0	0	749	76342	112	0	39.1	97.2	98.9	1.0	0.1
			S3	0	0	710	77296	83	0	39.6	98.3	99.0	0.9	0.1
			S4	0	0	691	76833	121	0	39.3	97.7	99.0	0.9	0.2
			Avg	0	0	712	77769	79	0	39.8	98.9	99.0	0.9	0.1
	1m	1.0	S1	0	0	791	76837	323	265	39.6	98.4	98.2	1.0	0.8
			S2	0	0	757	76578	296	199	39.4	97.9	98.4	1.0	0.6
			S3	0	0	772	77982	301	270	40.1	99.7	98.3	1.0	0.7
			S4	0	0	816	78440	298	255	40.3	100.3	98.3	1.0	0.7
			Avg	0	0	784	77459	305	247	39.9	99.1	98.3	1.0	0.7
	2m	2.1	S1	0	42	1108	84681	174	106	42.3	105.2	98.3	1.3	0.3
			S2	0	51	1036	78025	181	254	39.0	97.0	98.1	1.4	0.5
			S3	0	59	1049	79567	175	263	39.8	99.0	98.1	1.4	0.5
			S4	0	65	1093	78640	188	270	39.4	97.9	98.0	1.4	0.6
			Avg	0	54	1072	80228	180	223	40.1	99.8	98.1	1.4	0.5
	3m	3.0	S1	0	28	934	68868	314	297	39.5	98.2	97.8	1.4	0.9
			S2	0	19	1020	76176	297	229	43.3	107.6	98.0	1.3	0.7
			S3	0	23	961	72163	273	211	41.2	102.3	98.0	1.3	0.7
			S4	0	26	1005	69459	290	266	39.8	99.0	97.8	1.5	0.8
			Avg	0	24	980	71667	294	251	40.9	101.8	97.9	1.4	0.7
	4m	3.9	S1	0	86	1429	82496	302	330	41.0	102.0	97.5	1.8	0.7
			S2	0	63	1299	76942	258	250	38.2	94.9	97.6	1.7	0.6
			S3	0	41	1327	78887	245	209	39.1	97.2	97.7	1.7	0.6
			S4	0	43	1394	78762	273	254	39.1	97.3	97.6	1.8	0.7
			Avg	0	58	1362	79272	270	261	39.4	97.9	97.6	1.7	0.7
	5m	4.9	S1	0	66	1285	74405	479	421	40.1	99.6	97.1	1.8	1.2
			S2	0	61	1266	73140	428	384	39.3	97.8	97.2	1.8	1.1
			S3	0	57	1289	73762	444	405	39.7	98.7	97.1	1.8	1.1
			S4	0	76	1390	73395	459	409	39.6	98.4	96.9	1.9	1.1
			Avg	0	65	1308	73676	453	405	39.7	98.6	97.1	1.8	1.1
	6m	6.0	S1	0	69	1530	77628	445	449	40.9	101.7	96.9	2.0	1.1
			S2	0	45	1396	75253	379	338	39.5	98.2	97.2	1.9	0.9
			S3	0	54	1450	75700	415	408	39.8	99.0	97.0	1.9	1.1
			S4	0	72	1545	75933	391	347	40.0	99.3	97.0	2.1	0.9
			Avg	0	60	1480	76129	408	386	40.0	99.5	97.0	2.0	1.0
	31m	31.3	S1							41.546	103.3	83.79	13.28	2.92
			S2							42.043	104.5	83.66	13.44	2.9
			S3							40.336	100.3	83.92	13.23	2.85
			S4							40.948	101.8	82.7	14.42	2.88
			Avg							41.2	102.5	83.5	13.6	2.9

#6	t=0	0.0	S1	0	0	598	80845	0	0	42.4	100.0	99.3	0.7	0.0
			S2	0	0	510	74541	0	0	39.0	100.0	99.3	0.7	0.0
			S3	0	0	549	74683	0	0	39.1	100.0	99.3	0.7	0.0
			S4	0	0	497	75679	0	0	39.6	100.0	99.3	0.7	0.0
			Avg	0	0	539	76437	0	0	40.0	100.0	99.3	0.7	0.0
	0.5	0.5	S1	0	0	741	81916	122	0	42.0	105.0	99.0	0.9	0.1
			S2	0	0	668	76548	144	0	39.2	97.9	99.0	0.9	0.2
			S3	0	0	716	78512	0	0	40.2	100.4	99.1	0.9	0.0
			S4	0	0	634	75760	0	0	38.7	96.7	99.2	0.8	0.0
			Avg	0	0	690	78184	67	0	40.0	100.0	99.0	0.9	0.1
	1m	1.0	S1	0	0	789	80326	285	249	41.2	103.0	98.4	1.0	0.7
			S2	0	0	744	77807	313	232	40.0	100.0	98.4	0.9	0.7
			S3	0	0	785	78291	322	300	40.3	100.7	98.2	1.0	0.8
			S4	0	0	811	79104	334	307	40.7	101.7	98.2	1.0	0.8
			Avg	0	0	782	78882	314	272	40.6	101.4	98.3	1.0	0.7
	2m	2.1	S1	0	69	1057	80340	150	133	40.1	100.3	98.3	1.4	0.3
			S2	0	91	1075	78917	157	279	39.5	98.8	98.0	1.4	0.5
			S3	0	21	1043	79395	185	262	39.7	99.3	98.1	1.3	0.6
			S4	0	46	1086	80729	161	209	40.4	100.9	98.2	1.4	0.4
			Avg	0	57	1065	79845	163	221	39.9	99.8	98.1	1.4	0.5
	3m	3.0	S1	152	778	1376	67056	160	0	39.0	97.5	96.5	3.3	0.2
			S2	0	24	1079	78960	322	305	44.8	112.0	97.9	1.4	0.8
			S3	0	26	1067	78160	296	197	44.3	110.8	98.0	1.4	0.6
			S4	0	21	900	65169	293	263	37.5	93.8	97.8	1.4	0.8
			Avg	38	212	1106	72336	268	191	41.4	103.5	97.6	1.8	0.6
	4m	3.9	S1	0	49	1344	80031	298	349	39.8	99.4	97.5	1.7	0.8
			S2	0	43	1276	77367	247	210	38.4	95.9	97.8	1.7	0.6
			S3	0	47	1284	79151	252	191	39.2	98.0	97.8	1.6	0.5
			S4	0	50	1377	78578	248	209	39.0	97.5	97.7	1.8	0.6
			Avg	0	47	1320	78782	261	240	39.1	97.7	97.7	1.7	0.6
	5m	4.9	S1	0	52	1319	76420	461	349	41.1	102.6	97.2	1.7	1.0
			S2	0	35	1237	73249	376	351	39.3	98.3	97.3	1.7	1.0
			S3	0	54	1232	73682	410	299	39.5	98.8	97.4	1.7	0.9
			S4	0	63	1303	74816	397	324	40.2	100.4	97.3	1.8	0.9
			Avg	0	51	1273	74542	411	331	40.0	100.0	97.3	1.7	1.0
	6m	6.0	S1	0	64	1490	75108	412	399	39.5	98.8	96.9	2.0	1.0
			S2	0	50	1412	75096	374	340.0	39.4	98.5	97.2	1.9	0.9
			S3	0	47	1399	72982	399	412	38.3	95.8	97.0	1.9	1.1
			S4	0	52	1410	74952	388	379	39.4	98.4	97.1	1.9	1.0
			Avg	0	53	1428	74535	393	383	39.2	97.9	97.1	1.9	1.0
	31m	31.3	S1							42.085	105.2	85.41	11.88	2.71
			S2							40.995	102.5	85.34	11.83	2.84
			S3							40.995	102.5	85.13	12.23	2.64
			S4							40.607	101.5	85.86	11.26	2.88
			Avg							41.2	102.9	85.4	11.8	2.8

#7	t=0		S1	0	0	412	77578	0	0	40.6	100.0	99.5	0.5	0.0
			S2	0	0	376	76712	0	0	40.1	100.0	99.5	0.5	0.0
			Avg	0	0	394	77145	0	0	40.3	100.0	99.5	0.5	0.0
	0.5m		S1	0	0	696	78834	0	0	40.3	100.0	99.1	0.9	0.0
			S2	0	0	645	77392	705	0	39.9	99.0	98.3	0.8	0.9
			Avg	0	0	671	78113	353	0	40.1	99.5	98.7	0.8	0.4
	1m		S1	0	0	716	77017	390	312	39.7	98.4	98.2	0.9	0.9
			S2	0	0	682	79541	367	316	40.9	101.4	98.3	0.8	0.8
			Avg	0	0	699	78279	379	314	40.3	99.9	98.3	0.9	0.9
	2m		S1	0	74	1081	82027	172	235	41.1	101.8	98.1	1.4	0.5
			S2	0	25	991	79508	195	243	39.7	98.6	98.2	1.3	0.5
			Avg	0	50	1036	80768	184	239	40.4	100.2	98.2	1.3	0.5
	3m		S1	0	24	994	80283	346	289	45.5	112.8	98.0	1.2	0.8
			S1(re run)	0	75	1037	68237	285	197	40.4	100.2	97.7	1.6	0.7
			S2	0	14	827	69058	315	253	39.5	98.0	98.0	1.2	0.8
			Avg	0	38	953	72526	315	246	41.4	102.7	97.9	1.3	0.8
	4m		S1	0	344	745	82388	58	0	40.5	100.5	98.6	1.3	0.1
			Avg	0	344	745	82388	58	0	40.5	101.2	98.6	1.3	0.1
	5m		S1	0	82	1176	71477	433	399	38.5	95.4	97.2	1.7	1.1
			S2	0	40	1187	73435	448	544	39.5	98.1	97.1	1.6	1.3
			avg	0	61	1182	72456	441	472	39.0	96.7	97.1	1.7	1.2
	6m		S1	0	47	1406	77409	454	470	40.7	101.1	97.0	1.8	1.2
			S2	0	56	1330	76005	416	445	39.9	99.1	97.1	1.8	1.1
			avg	0	52	1368	76707	435	458	40.3	100	97.1	2	1
	31m		S1							39.794	98.7	86.4	10.95	2.7

t=0 seq 060117F
t=0.5m, 5C, seq 060128G
t=1m, seq 060214G
t=2m, seq 060322E
t=3m seq 060426X
d6s1 3m, rerun, seq 060501X

t=4m, seq 060524H
t=5m seq 060613GA
t=6m 060720B

Sequence		SE-HPLC C-ISO method	working STD lot	working STD conc	slope	int	injection volume (uL)	Corr Coef	% STD deviation	Sample IDs	Cal ID
080827 Pam		NA	EF-7630-13	10mg/mL	3.93E+06	-3.77E+05	0.5	0.9997		D1-7 25C 31m	17273

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Stability Study VGFT-SS207 Syringe Stress, Vtx, FT

Device	Length of Stress (DAYS)	Replicate #	HMW Peak Area	HMW Peak Area	HMW Peak Area	Native Peak Area	LMW Peak Area	LMW Peak Area	[VEGF-TRAP] mg/ml	% VEGF-TRAP Recov-ered	% Native VEGF-TRAP	% HMW Species	% LMW Species
#7 (vial)	T=0	R1	0	0	412	77578	0	0	40.6	100.0	99.5	0.5	0.0
	(from thermal data)	R2	0	0	376	76712	0	0	40.1	100.0	99.5	0.5	0.0
		Avg	0	0	394	77145	0	0	40.3	100.0	99.5	0.5	0.0
	Seq 060515F												
	1X Syr 1mL	R1	0	0	410	75841	0	0	38.6	95.8	99.5	0.5	0.0
	4X Syr 1mL	R1	0	0	427	77605	0	0	39.6	98.2	99.5	0.5	0.0

Stability Study VGFT-SS207 -40ºC

Device	Length of stress (days)	Syringe	HMW Peak Area	HMW Peak Area	HMW Peak Area	Native Peak Area	LMW Peak Area	LMW Peak Area	[VEGF-TRAP] mg/ml	% VEGF-TRAP Recov-ered	% Native VEGF-TRAP	% HMW Species	% LMW Species
#1	t=0	S1	0	0	549	80482	0	0	42.2	100.0	99.3	0.7	0.0
		S2	0	0	497	73534	0	0	38.4	100.0	99.3	0.7	0.0
		S3	0	0	499	76050	0	0	39.8	100.0	99.3	0.7	0.0
		S4	0	0	490	75245	0	0	39.3	100.0	99.4	0.6	0.0
		Avg	0	0	509	76328	0	0	39.9	100.0	99.3	0.7	0.0
#2	t=0	S1	0	0	527	78972	0	0	41.4	100.0	99.3	0.7	0.0
		S2	0	0	478	74712	0	0	39.1	100.0	99.4	0.6	0.0
		S3	0	0	479	76710	0	0	40.1	100.0	99.4	0.6	0.0
		S4	0	0	478	76037	0	0	39.8	100.0	99.4	0.6	0.0
		Avg	0	0	491	76608	0	0	40.1	100.0	99.4	0.6	0.0
#3	t=0	S1	0	0	498	78967	0	0	41.3	100.0	99.4	0.6	0.0
		S2	0	0	451	74099	0	0	38.7	100.0	99.4	0.6	0.0
		S3	0	0	472	75574	0	0	39.5	100.0	99.4	0.6	0.0
		S4	0	0	482	75293	0	0	39.4	100.0	99.4	0.6	0.0
		Avg	0	0	476	75983	0	0	39.7	100.0	99.4	0.6	0.0

	10m	S1	0	0	472	77974	0	0	39.2	98.6	99.4	0.6	0.0
		S2	0	0	493	81197	0	0	40.7	102.3	99.4	0.6	0.0
		Avg	0	0	483	79586	0	0	40	100	99	1	0
#4	t=0	S1	0	0	532	79812	0	0	41.8	100.0	99.3	0.7	0.0
		S2	0	0	464	75433	0	0	39.4	100.0	99.4	0.6	0.0
		S3	0	0	486	75338	0	0	39.4	100.0	99.4	0.6	0.0
		S4	0	0	503	76975	0	0	40.3	100.0	99.4	0.6	0.0
		Avg	0	0	496	76890	0	0	40.2	100.0	99.4	0.6	0.0

#5	t=0	S1	0	0	509	79339	0	0	41.5	100.0	99.4	0.6	0.0
		S2	0	0	492	75410	0	0	39.4	100.0	99.4	0.6	0.0
		S3	0	0	530	77056	0	0	40.3	100.0	99.3	0.7	0.0
		S4	0	0	474	75743	0	0	39.6	100.0	99.4	0.6	0.0
		Avg	0	0	501	76887	0	0	40.2	100.0	99.4	0.6	0.0
#6	t=0	S1	0	0	598	80845	0	0	42.4	100.0	99.3	0.7	0.0
		S2	0	0	510	74541	0	0	39.0	100.0	99.3	0.7	0.0
		S3	0	0	549	74683	0	0	39.1	100.0	99.3	0.7	0.0
		S4	0	0	497	75679	0	0	39.6	100.0	99.3	0.7	0.0
		Avg	0	0	539	76437	0	0	40.0	100.0	99.3	0.7	0.0
#7	t=0	S1	0	0	412	77578	0	0	40.6	100.0	99.5	0.5	0.0
		S2	0	0	376	76712	0	0	40.1	100.0	99.5	0.5	0.0
		Avg	0	0	394	77145	0	0	40.3	100.0	99.5	0.5	0.0
	10m	v1	0	0	355	79259	0	0	39.7	98.5	99.6	0.4	0.0
		v2	0	0	379	79883	0	0	40.0	99.2	99.5	0.5	0.0
		Avg	0	0	367	79571	0	0	40	99	100	0	0

t=0 seq 060117F
10m D3, D7 Seq 061115K

VEGFT-SS207 End of Study SEC analysis
Device 3 and Device 7 (Control Vial)

Export line #	Sample ID	Cal ID	Result ID	Conc	Total Agg (%)	Native (%)	Total Deg (%)	VEGFT Recovered (%)	Device	Stress (months)	Syringe
3	03 EF-7630-13 10mg/mL 10ug	9388	9408	10	2.70	**96.89**	0.00				
4	03 EF-7630-13 10mg/mL 15ug	9388	9407	10	2.28	**97.72**	0.00				
5	03 EF-7630-13 10mg/mL 20ug	9388	9406	10	2.31	**97.69**	0.00				
6	03 EF-7630-13 10mg/mL 20ug	9388	9405	10	2.32	**97.68**	0.00				
7	03 EF-7630-13 10mg/mL 20ug	9388	9404	10	2.32	**97.68**	0.00				
8	03 EF-7630-13 10mg/mL 20ug	9388	9403	10	2.33	**97.67**	0.00				
9	03 EF-7630-13 10mg/mL 25ug	9388	9402	10	2.34	**97.66**	0.00				
10	03 EF-7630-13 10mg/mL 30ug	9388	9401	10	2.33	**97.66**	0.00				
25	03 EF-7630-13 10mg/mL 10ug	9388	9409	10	2.47	**96.30**	0.00				
26	03 EF-7630-13 10mg/mL 15ug	9388	9400	10	2.03	**97.97**	0.00				
27	03 EF-7630-13 10mg/mL 20ug	9388	9399	10	2.15	**97.85**	0.00				
28	03 EF-7630-13 10mg/mL 20ug	9388	9414	10	2.20	**97.79**	0.00				
29	03 EF-7630-13 10mg/mL 20ug	9388	9413	10	2.19	**97.79**	0.00				
30	03 EF-7630-13 10mg/mL 20ug	9388	9412	10	2.19	**97.81**	0.00				
31	03 EF-7630-13 10mg/mL 25ug	9388	9411	10	2.21	**97.76**	0.00				
32	03 EF-7630-13 10mg/mL 30ug	9388	9410	10	2.22	**97.75**	0.00				
103	03 EF-7630-13 10mg/mL 20ug	9388	9415	8.221	2.16	**97.84**	0.00	*Wrong inj vol (0.2uL)*			
119	03 EF-7630-13 10mg/mL 20ug	9388	9527	8.274	2.14	**97.86**	0.00	*Wrong inj vol (0.2uL)*			
134	03 EF-7630-13 10mg/mL 20ug	9388	9512	7.785	1.94	**98.06**	0.00	*Wrong inj vol (0.2uL)*			
5	03 EF-7630-13 10mg/mL 20ug	9388	9733	9.925	2.21	**97.79**	0.00				
18	03 EF-7630-13 10mg/mL 20ug	9388	9747	9.878	2.16	**97.84**	0.00				
32	03 EF-7630-13 10mg/mL 20ug	9388	9761	9.915	2.19	**97.81**	0.00				
7	03 EF-7630-13 10mg/mL 20ug	9388	9844	9.876	2.19	**97.81**	0				
18	03 EF-7630-13 10mg/mL 20ug	9388	9845	9.962	2.2	**97.8**	0				

Sequence	SE-HPLC C-ISO method	working STD conc	working STD lot	Cal ID	slope	int	injection Amount	Corr Coef	% STD dev
080220 Max	CISO	10 mg/mL	EF-7630-13	9388	3678749	1971811	20ug	0.9988	

VEGFT-SS207 End of Study SEC analysis
Device 3 and Device 7 (Control Vial) t=0

Export line #	Sample ID	Cal ID	Result ID	Conc	Total Agg (%)	Native (%)	Total Deg (%)	VEGFT Recovered (%)	Device	t=0 Stress	Syringe / rep #
11	03 S207 t=0 D3 r2 set1	9388	9503	39.346	0.79	**99.21**	0.00	99.6	**3**	**t=0**	2.0
12	03 S207 t=0 D3 r3 set1	9388	9502	38.814	0.78	**99.22**	0.00	100.5	**3**	**t=0**	3.0
13	03 S207 t=0 D3 r4 set1	9388	9501	38.371	0.76	**99.24**	0.00	99.0	**3**	**t=0**	4.0
14	03 S207 t=0 D3 r5 set2	9388	9500	41.302	0.77	**99.23**	0.00	99.6	**3**	**t=0**	5.0
3	03 S207 t=0 D3 r2 set1	9388	9730	39.669	0.88	**99.12**	0.00	100.4	**3**	**t=0**	2.0
4	03 S207 t=0 D3 r3 set1	9388	9731	38.39	0.87	**99.13**	0.00	99.5	**3**	**t=0**	3.0
6	03 S207 t=0 D3 r4 set1	9388	9735	39.141	0.86	**99.14**	0.00	101.0	**3**	**t=0**	4.0
7	03 S207 t=0 D3 r5 set2	9388	9736	41.664	0.90	**99.10**	0.00	100.4	**3**	**t=0**	5.0
Avg	*03 S207 t=0 D3 r2 set1*			*39.5075*	*0.84*	***99.17***	*0.00*	*100.0*	***3***	***t=0***	*2.0*
Avg	*03 S207 t=0 D3 r3 set1*			*38.602*	*0.83*	***99.18***	*0.00*	*100.0*	***3***	***t=0***	*3.0*
Avg	*03 S207 t=0 D3 r4 set1*			*38.756*	*0.81*	***99.19***	*0.00*	*100.0*	***3***	***t=0***	*4.0*
Avg	*03 S207 t=0 D3 r5 set2*			*41.483*	*0.84*	***99.17***	*0.00*	*100.0*	***3***	***t=0***	*5.0*
Avg	***VGFT-SS207 t=0 D3***			***39.59***	***0.83***	***99.17***	***0.00***	***100.0***	***3***	***t=0***	***All***
15	03 S207 t=0 D7 r1 set1	9388	9499	41.252	1.00	**99.00**	0.00	105.4	**7**	**t=0**	1.0
16	03 S207 t=0 D7 r2 set1	9388	9498	40.06	0.86	**99.14**	0.00	101.1	**7**	**t=0**	2.0
17	03 S207 t=0 D7 r3 set1	9388	9497	38.901	0.91	**99.09**	0.00	101.2	**7**	**t=0**	3.0
18	03 S207 t=0 D7 r4 set2	9388	9496	39.701	0.52	**99.48**	0.00	98.6	**7**	**t=0**	4.0
8	03 S207 t=0 D7 r1 set1	9388	9737	36.997	1.26	**98.74**	0.00	94.6	**7**	**t=0**	1.0
9	03 S207 t=0 D7 r2 set1	9388	9738	39.189	1.06	**98.94**	0.00	98.9	**7**	**t=0**	2.0
10	03 S207 t=0 D7 r3 set1	9388	9739	37.946	1.04	**98.96**	0.00	98.8	**7**	**t=0**	3.0
11	03 S207 t=0 D7 r4 set2	9388	9740	40.796	0.70	**99.30**	0.00	101.4	**7**	**t=0**	4.0
Avg	*03 S207 t=0 D7 r1 set1*			*39.1245*	*1.13*	***98.87***	*0.00*	*100.0*	***7***	***t=0***	*1.0*
Avg	*03 S207 t=0 D7 r2 set1*			*39.6245*	*0.96*	***99.04***	*0.00*	*100.0*	***7***	***t=0***	*2.0*
Avg	*03 S207 t=0 D7 r3 set1*			*38.4235*	*0.98*	***99.03***	*0.00*	*100.0*	***7***	***t=0***	*3.0*
Avg	*03 S207 t=0 D7 r4 set2*			*40.2485*	*0.61*	***99.39***	*0.00*	*100.0*	***7***	***t=0***	*4.0*
Avg	***VGFT-SS207 t=0 D7***			***39.36***	***0.92***	***99.08***	***0.00***	***100.0***	***7***	***t=0***	***All***

VEGFT-SS207 End of Study SEC analysis
Device 3 and Device 7 (Control Vial) 25C

Export line #	Sample ID	Cal ID	Result ID	Conc	Total Agg (%)	Native (%)	Total Deg (%)	VEGFT Recovered (%)	Device	25ºC Stress (months)	Syringe / rep #
33	03 SS207 25C 0.5m D3 S1	9388	9488	45.448	1.24	**98.76**	0.00	114.8	**3**	**0.5m**	1
34	03 SS207 25C 0.5m D3 S2	9388	9487	38.519	0.93	**99.07**	0.00	97.3	**3**	**0.5m**	2
35	03 SS207 25C 0.5m D3 S3	9388	9486	37.888	0.96	**99.04**	0.00	95.7	**3**	**0.5m**	3
36	03 SS207 25C 0.5m D3 S4	9388	9485	38.393	0.80	**99.20**	0.00	97.0	**3**	**0.5m**	4
					0.98	***99.02***					
37	03 SS207 25C 0.5m D7 R1	9388	9484	40.341	0.99	**99.01**	0.00	102.5	**7**	**0.5m**	1
38	03 SS207 25C 0.5m D7 R2	9388	9483	38.824	1.01	**98.99**	0.00	98.7	**7**	**0.5m**	2
39	03 SS207 25C 1m D3 S1	9388	9482	39.574	1.06	**98.91**	0.02	100.0	**3**	**1m**	1
40	03 SS207 25C 1m D3 S2	9388	9481	40.894	1.12	**98.84**	0.04	103.3	**3**	**1m**	2
41	03 SS207 25C 1m D3 S3	9388	9480	38.942	1.06	**98.89**	0.05	98.4	**3**	**1m**	3
42	03 SS207 25C 1m D3 S4	9388	9479	40.349	1.15	**98.82**	0.04	101.9	**3**	**1m**	4
					1.10	***98.87***					
43	03 SS207 25C 1m D7 R1	9388	9478	39.069	0.98	**98.96**	0.06	99.3	**7**	**1m**	1
44	03 SS207 25C 1m D7 R2	9388	9477	38.452	1.01	**98.96**	0.03	97.7	**7**	**1m**	2
45	03 SS207 25C 2m D3 S1	9388	9476	38.882	1.31	**98.58**	0.12	98.2	**3**	**2m**	1
46	03 SS207 25C 2m D3 S2	9388	9475	39.768	1.41	**98.49**	0.10	100.5	**3**	**2m**	2
47	03 SS207 25C 2m D3 S3	9388	9474	40.197	1.30	**98.62**	0.08	101.5	**3**	**2m**	3
48	03 SS207 25C 2m D3 S4	9388	9473	38.588	1.24	**98.64**	0.12	97.5	**3**	**2m**	4
					1.32	***98.58***					
49	03 SS207 25C 2m D7 R1	9388	9472	44.686	1.56	**98.33**	0.11	113.5	**7**	**2m**	1
50	03 SS207 25C 2m D7 R2	9388	9471	39.892	1.39	**98.49**	0.13	101.4	**7**	**2m**	2
51	03 SS207 25C 3m D3 S1	9388	9470	38.863	1.49	**98.35**	0.16	98.2	**3**	**3m**	1
52	03 SS207 25C 3m D3 S2	9388	9469	38.73	1.55	**98.28**	0.17	97.8	**3**	**3m**	2
53	03 SS207 25C 3m D3 S3	9388	9468	35.544	1.45	**98.38**	0.17	89.8	**3**	**3m**	3
54	03 SS207 25C 3m D3 S4	9388	9467	39.048	1.51	**98.32**	0.18	98.6	**3**	**3m**	4
					1.50	***98.33***					
55	03 SS207 25C 3m D7 R1	9388	9466	40.118	1.43	**98.38**	0.19	101.9	**7**	**3m**	1
56	03 SS207 25C 3m D7 R2	9388	9465	36.976	1.41	**98.40**	0.20	94.0	**7**	**3m**	2
57	03 SS207 25C 4m D3 S1	9388	9464	39.809	1.66	**98.12**	0.22	100.6	**3**	**4m**	1
58	03 SS207 25C 4m D3 S2	9388	9463	40.751	1.83	**97.98**	0.20	102.9	**3**	**4m**	2
59	03 SS207 25C 4m D3 S3	9388	9462	41.009	1.71	**98.10**	0.19	103.6	**3**	**4m**	3
60	03 SS207 25C 4m D3 S4	9388	9458	37.94	1.67	**98.10**	0.23	95.8	**3**	**4m**	4
					1.72	***98.08***					
61	03 SS207 25C 4m D7 R1	9388	9457	39.898	1.75	**98.01**	0.25	101.4	**7**	**4m**	1
62	03 SS207 25C 4m D7 R2	9388	9456	39.645	1.84	**97.92**	0.24	100.7	**7**	**4m**	2
63	03 SS207 25C 5m D3 S1	9388	9455	39.522	1.85	**97.88**	0.27	99.8	**3**	**5m**	1
64	03 SS207 25C 5m D3 S2	9388	9454	40.09	1.95	**97.79**	0.26	101.3	**3**	**5m**	2
65	03 SS207 25C 5m D3 S3	9388	9453	36.115	1.88	**97.83**	0.26	91.2	**3**	**5m**	3
66	03 SS207 25C 5m D3 S4	9388	9452	38.791	1.88	**97.85**	0.26	98.0	**3**	**5m**	4
					1.89	***97.84***					
67	03 SS207 25C 5m D7 R1	9388	9451	39.065	1.80	**97.90**	0.30	99.3	**7**	**5m**	1
68	03 SS207 25C 5m D7 R2	9388	9450	37.924	1.73	**97.97**	0.30	96.4	**7**	**5m**	2
69	03 SS207 25C 6m D3 S1	9388	9449	38.809	1.98	**97.68**	0.34	98.0	**3**	**6m**	1
70	03 SS207 25C 6m D3 S2	9388	9448	39.202	2.02	**97.62**	0.33	99.0	**3**	**6m**	2
71	03 SS207 25C 6m D3 S3	9388	9447	38.135	2.05	**97.62**	0.33	96.3	**3**	**6m**	3
72	03 SS207 25C 6m D3 S4	9388	9446	38.894	2.08	**97.59**	0.33	98.2	**3**	**6m**	4
					2.03	***97.63***					
73	03 SS207 25C 6m D7 R1	9388	9445	39.417	2.14	**97.51**	0.35	100.2	**7**	**6m**	1
23	03 SS207 25C ~~5C~~ 6m D7 R1	9388	9752	38.261	2.08	**97.54**	0.38	97.2	**7**	**6m**	1
Avg	*03 SS207 25C 6m D7 R1*			*38.839*	*2.11*	***97.53***	*0.37*	*98.7*	***7***	***6m***	*1*
74	03 SS207 25C 6m D7 R3	9388	9444	39.126	1.98	**97.64**	0.36	99.4	**7**	**6m**	3
24	03 SS207 25C ~~5C~~ 6m D7 R3	9388	9753	40.077	2.21	**97.41**	0.38	101.8	**7**	**6m**	3
Avg	*03 SS207 25C 6m D7 R3*			*39.6015*	*2.10*	***97.53***	*0.37*	*100.6*	***7***	***6m***	*3*

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VEGFT-SS207 End of Study SEC analysis
Device 3 and Device 7 (Control Vial) 37C

Export line #	Sample ID	Cal ID	Result ID	Conc	Total Agg (%)	Native (%)	Total Deg (%)	VEGFT Recovered (%)	Device	37ºC Stress (days)	Syringe / rep #
89	03 SS207 37C 7d D3 S1	9388	9429	38.233	2.22	**97.70**	0.07	96.6	**3**	**7d**	1
90	03 SS207 37C 7d D3 S2	9388	9428	39.065	2.35	**97.55**	0.10	98.7	**3**	**7d**	2
91	03 SS207 37C 7d D3 S3	9388	9427	39.929	2.48	**97.45**	0.07	100.9	**3**	**7d**	3
92	03 SS207 37C 7d D3 S4	9388	9426	39.484	2.47	**97.47**	0.06	99.7	**3**	**7d**	4
93	03 SS207 37C 7d D7 R1	9388	9425	39.788	2.42	**97.46**	0.12	101.1	**7**	**7d**	1
94	03 SS207 37C 7d D7 R2	9388	9424	40.342	2.55	**97.37**	0.08	102.5	**7**	**7d**	2
95	03 SS207 37C 7d D7 R3	9388	9423	41.046	2.52	**97.35**	0.12	104.3	**7**	**7d**	3
19	03 SS207 37C 14d D3 S1	9388	9495	38.753	3.37	**96.38**	0.16	97.9	**3**	**14d**	1
20	03 SS207 37C 14d D3 S2	9388	9494	39.158	3.51	**96.22**	0.16	98.9	**3**	**14d**	2
21	03 SS207 37C 14d D3 S3	9388	9493	42.8	3.84	**95.76**	0.15	108.1	**3**	**14d**	3
22	03 SS207 37C 14d D3 S4	9388	9492	41.537	4.39	**95.21**	0.15	104.9	**3**	**14d**	4
23	03 SS207 37C 14d D7 R1	9388	9491	44.261	4.56	**94.79**	0.18	112.5	**7**	**14d**	1
24	03 SS207 37C 14d D7 R2	9388	9490	38.877	4.05	**95.60**	0.21	98.8	**7**	**14d**	2
	03 SS207 37C 14d D7 R3										
75	03 SS207 37C 14d D3 S1	9388	9443	38.733	3.50	**96.28**	0.17	97.8	**3**	**14d**	1
96	03 SS207 37C 14d D3 S2	9388	9422	39.437	3.63	**96.13**	0.18	99.6	**3**	**14d**	2
97	03 SS207 37C 14d D3 S3	9388	9421	38.816	3.83	**95.88**	0.16	98.1	**3**	**14d**	3
98	03 SS207 37C 14d D3 S4	9388	9420	39.281	4.27	**95.41**	0.17	99.2	**3**	**14d**	4
99	03 SS207 37C 14d D7 R1	9388	9419	40.812	4.14	**95.49**	0.21	103.7	**7**	**14d**	1
100	03 SS207 37C 14d D7 R2	9388	9418	39.518	4.12	**95.53**	0.23	100.4	**7**	**14d**	2
101	03 SS207 37C 14d D7 R3	9388	9417	38.956	4.24	**95.39**	0.21	99.0	**7**	**14d**	3
Avg	*03 SS207 37C 14d D3 S1*			*38.743*	*3.44*	***96.33***	*0.165*	*97.9*	***3***	***14d***	*1*
Avg	*03 SS207 37C 14d D3 S2*			*39.2975*	*3.57*	***96.175***	*0.17*	*99.3*	***3***	***14d***	*2*
Avg	*03 SS207 37C 14d D3 S3*			*40.808*	*3.835*	***95.82***	*0.155*	*103.1*	***3***	***14d***	*3*
Avg	*03 SS207 37C 14d D3 S4*			*40.409*	*4.33*	***95.31***	*0.16*	*102.1*	***3***	***14d***	*4*
Avg	*03 SS207 37C 14d D7 R1*			*42.5365*	*4.35*	***95.14***	*0.195*	*108.1*	***7***	***14d***	*1*
Avg	*03 SS207 37C 14d D7 R2*			*39.1975*	*4.085*	***95.565***	*0.22*	*99.6*	***7***	***14d***	*2*
76	03 SS207 37C 21d D3 S1	9388	9442	42.091	4.93	**94.65**	0.15	106.3	**3**	**21d**	1
77	03 SS207 37C 21d D3 S2	9388	9441	39.055	4.70	**94.91**	0.24	98.7	**3**	**21d**	2
78	03 SS207 37C 21d D3 S3	9388	9440	39.102	4.66	**94.92**	0.24	98.8	**3**	**21d**	3
79	03 SS207 37C 21d D3 S4	9388	9439	38.276	5.48	**94.02**	0.25	96.7	**3**	**21d**	4
80	03 SS207 37C 21d D7 R1	9388	9438	39.908	5.53	**94.47**	0.00	101.4	**7**	**21d**	1
81	03 SS207 37C 21d D7 R2	9388	9437	38.942	5.70	**93.70**	0.30	98.9	**7**	**21d**	2
82	03 SS207 37C 21d D7 R3	9388	9436	38.906	5.68	**93.72**	0.30	98.9	**7**	**21d**	3
83	03 SS207 37C 28d D3 S1	9388	9435	38.128	5.99	**93.38**	0.29	96.3	**3**	**28d**	1
84	03 SS207 37C 28d D3 S2	9388	9434	38.783	6.03	**93.34**	0.31	98.0	**3**	**28d**	2
85	03 SS207 37C 28d D3 S3	9388	9433	39.509	6.76	**92.36**	0.29	99.8	**3**	**28d**	3
86	03 SS207 37C 28d D7 R1	9388	9432	40.902	7.12	**92.18**	0.00	103.9	**7**	**28d**	1
87	03 SS207 37C 28d D7 R2	9388	9431	41.126	7.12	**91.88**	0.36	104.5	**7**	**28d**	2
88	03 SS207 37C 28d D7 R3	9388	9430	39.234	7.01	**91.95**	0.35	99.7	**7**	**28d**	3

VEGFT-SS207 End of Study SEC analysis
Device 3 and Device 7 (Control Vial) 5C

Export line #	Sample ID	Cal ID	Result ID	Conc	Total Agg (%)	Native (%)	Total Deg (%)	VEGFT Recovered (%)	Device	5ºC Stress (months)	Syringe / rep #
106	03 SS207 5C 0.5m D3 S1	9388	9540	40.606	0.83	**99.17**	0.00	102.6	**3**	**0.5m**	1
107	03 SS207 5C 0.5m D3 S2	9388	9539	38.254	0.73	**99.23**	0.00	96.6	**3**	**0.5m**	2
108	03 SS207 5C 0.5m D3 S4	9388	9538	39.563	0.69	**99.31**	0.00	99.9	**3**	**0.5m**	4
109	03 SS207 5C 0.5m D7 R1	9388	9537	41.338	0.77	**99.23**	0.00	105.0	**7**	**0.5m**	1
110	03 SS207 5C 0.5m D7 R2	9388	9536	2.1	1.57	**98.43**	0.00	5.3	**7**	**0.5m**	2
111	03 SS207 5C 0.5m D7 R3	9388	9535	38.394	0.75	**99.22**	0.00	97.6	**7**	**0.5m**	3
112	03 SS207 5C 1m D3 S1	9388	9534	40.62	1.00	**99.00**	0.00	102.6	**3**	**1m**	1
113	03 SS207 5C 1m D3 S2	9388	9533	39.417	0.87	**99.13**	0.00	99.6	**3**	**1m**	2
114	03 SS207 5C 1m D3 S3	9388	9532	39.188	0.91	**99.09**	0.00	99.0	**3**	**1m**	3
115	03 SS207 5C 1m D3 S4	9388	9531	41.237	0.93	**99.07**	0.00	104.2	**3**	**1m**	4
116	03 SS207 5C 1m D7 R1	9388	9530	41.042	0.72	**99.28**	0.00	104.3	**7**	**1m**	1
117	03 SS207 5C 1m D7 R2	9388	9529	38.824	0.71	**99.27**	0.00	98.7	**7**	**1m**	2
118	03 SS207 5C 1m D7 R3	9388	9528	37.721	0.66	**99.32**	0.00	95.8	**7**	**1m**	3
120	03 SS207 5C 2m D3 S1	9388	9526	39.56	0.74	**99.26**	0.00	99.9	**3**	**2m**	1
121	03 SS207 5C 2m D3 S2	9388	9525	40.235	0.86	**99.14**	0.00	101.6	**3**	**2m**	2
122	03 SS207 5C 2m D3 S3	9388	9524	40.77	0.88	**99.12**	0.00	103.0	**3**	**2m**	3
123	03 SS207 5C 2m D3 S4	9388	9523	38.753	0.75	**99.25**	0.00	97.9	**3**	**2m**	4
124	03 SS207 5C 2m D7 R1	9388	9522	39.837	0.87	**99.13**	0.00	101.2	**7**	**2m**	1
125	03 SS207 5C 2m D7 R2	9388	9521	40.628	0.93	**99.07**	0.00	103.2	**7**	**2m**	2
126	03 SS207 5C 2m D7 R3	9388	9520	40.562	0.93	**99.04**	0.00	103.1	**7**	**2m**	3
127	03 SS207 5C 3m D3 S1	9388	9519	42.081	0.93	**99.07**	0.00	106.3	**3**	**3m**	1
128	03 SS207 5C 3m D3 S2	9388	9518	35.75	0.84	**99.16**	0.00	90.3	**3**	**3m**	2
129	03 SS207 5C 3m D3 S3	9388	9517	39.053	0.82	**99.18**	0.00	98.7	**3**	**3m**	3
130	03 SS207 5C 3m D3 S4	9388	9516	39.57	0.76	**99.24**	0.00	100.0	**3**	**3m**	4
131	03 SS207 5C 3m D7 R1	9388	9515	40.864	0.69	**99.31**	0.00	103.8	**7**	**3m**	1
132	03 SS207 5C 3m D7 R2	9388	9514	41.244	0.81	**99.19**	0.00	104.8	**7**	**3m**	2
133	03 SS207 5C 3m D7 R3	9388	9513	39.988	0.87	**99.10**	0.00	101.6	**7**	**3m**	3
135	03 SS207 5C 4m D3 S1	9388	9511	42.102	0.96	**99.04**	0.00	106.4	**3**	**4m**	1
136	03 SS207 5C 4m D3 S2	9388	9510	40.033	0.87	**99.13**	0.00	101.1	**3**	**4m**	2
137	03 SS207 5C 4m D3 S3	9388	9509	39.699	0.99	**98.99**	0.00	100.3	**3**	**4m**	3
138	03 SS207 5C 4m D3 S4	9388	9508	39.609	0.94	**99.06**	0.00	100.1	**3**	**4m**	4
16	03 SS207 5C 4m D7 R1	9388	9846	41.492	3.42	**96.58**	0	105.4	**7**	**4m**	1
17	03 SS207 5C 4m D7 R3	9388	9847	39.046	0.83	**99.17**	0	99.2	**7**	**4m**	3
12	03 SS207 5C 5m D3 S1	9388	9741	39.19	0.87	**99.13**	0.00	99.0	**3**	**5m**	1
13	03 SS207 5C 5m D3 S2	9388	9742	40.022	0.79	**99.21**	0.00	101.1	**3**	**5m**	2
14	03 SS207 5C 5m D3 S3	9388	9743	38.735	0.86	**99.14**	0.00	97.8	**3**	**5m**	3
15	03 SS207 5C 5m D3 S4	9388	9744	39.338	0.87	**99.13**	0.00	99.4	**3**	**5m**	4
16	03 SS207 5C 5m D7 R1	9388	9745	40.123	1.04	**98.96**	0.00	102.0	**7**	**5m**	1
17	03 SS207 5C 5m D7 R3	9388	9746	39.215	0.87	**99.13**	0.00	99.6	**7**	**5m**	3
19	03 SS207 5C 6m D3 S1	9388	9748	37.852	1.00	**99.00**	0.00	95.6	**3**	**6m**	1
20	03 SS207 5C 6m D3 S2	9388	9749	39.365	0.88	**99.12**	0.00	99.4	**3**	**6m**	2
21	03 SS207 5C 6m D3 S3	9388	9750	39.233	0.92	**99.08**	0.00	99.1	**3**	**6m**	3
22	03 SS207 5C 6m D3 S4	9388	9751	39.321	0.92	**99.08**	0.00	99.3	**3**	**6m**	4
104	03 SS207 ~~25C~~ 5C 6m D7 R1	9388	9542	41.301	0.92	**99.08**	0.00	104.9	**7**	**6m**	1
105	03 SS207 ~~25C~~ 5C 6m D7 R2	9388	9541	40.768	0.83	**99.17**	0.00	103.6	**7**	**6m**	2
25	03 SS207 5C 9m D3 S1	9388	9754	46.837	1.42	**98.58**	0.00	118.3	**3**	**9m**	1
26	03 SS207 5C 9m D3 S2	9388	9755	39.293	0.99	**99.01**	0.00	99.3	**3**	**9m**	2
27	03 SS207 5C 9m D3 S3	9388	9756	39.777	1.20	**98.80**	0.00	100.5	**3**	**9m**	3
28	03 SS207 5C 9m D3 S4	9388	9757	39.355	1.05	**98.93**	0.02	99.4	**3**	**9m**	4
29	03 SS207 5C 9m D7 R1	9388	9758	39.84	0.96	**99.02**	0.02	101.2	**7**	**9m**	1
30	03 SS207 5C 9m D7 R3	9388	9759	40.346	0.94	**99.06**	0.00	102.5	**7**	**9m**	3
34	03 SS207 5C 12m D3 S1	9388	9763	41.094	1.25	**98.74**	0.01	103.8	**3**	**12m**	1
35	03 SS207 5C 12m D3 S2	9388	9764	38.321	0.99	**99.01**	0.00	96.8	**3**	**12m**	2
36	03 SS207 5C 12m D3 S3	9388	9765	39.079	0.97	**99.01**	0.02	98.7	**3**	**12m**	3
37	03 SS207 5C 12m D3 S4	9388	9766	38.768	0.98	**98.98**	0.04	97.9	**3**	**12m**	4
38	03 SS207 5C 12m D7 R1	9388	9767	39.699	0.93	**99.03**	0.04	100.9	**7**	**12m**	1
9	03 SS207 5C 15m D3 S1	9388	9830	37.542	1.14	**98.82**	0.05	94.8	**3**	**15m**	1
1	03 SS207 5C 15m D3 S2	9388	9831	38.672	1.09	**98.87**	0.04	97.7	**3**	**15m**	2
2	03 SS207 5C 15m D3 S3	9388	9832	39.16	1.09	**98.87**	0.05	98.9	**3**	**15m**	3
3	03 SS207 5C 15m D3 S4	9388	9833	38.097	1.06	**98.9**	0.04	96.2	**3**	**15m**	4
4	03 SS207 5C 15m D7 R1	9388	9834	46.635	1.57	**98.4**	0.04	118.5	**7**	**15m**	1
5	03 SS207 5C 15m D7 R2	9388	9835	40.645	1.12	**98.86**	0.02	103.3	**7**	**15m**	2
6	03 SS207 5C 18m D3 S1	9388	9836	37.988	1.15	**98.79**	0.05	96.0	**3**	**18m**	1
8	03 SS207 5C 18m D3 S2	9388	9837	38.31	1.11	**98.84**	0.05	96.8	**3**	**18m**	2
10	03 SS207 5C 18m D3 S3	9388	9838	38.824	1.13	**98.82**	0.05	98.1	**3**	**18m**	3
11	03 SS207 5C 18m D3 S4	9388	9839	39.351	1.1	**98.82**	0.08	99.4	**3**	**18m**	4
12	03 SS207 5C 18m D7 R1	9388	9840	40.023	1.29	**98.64**	0.07	101.7	**7**	**18m**	1
13	03 SS207 5C 24m D3 S1	9388	9841	40.579	1.32	**98.59**	0.09	102.5	**3**	**24m**	1
14	03 SS207 5C 24m D3 S4	9388	9842	39.003	1.29	**98.64**	0.06	98.5	**3**	**24m**	4
15	03 SS207 5C 24m D7 R1	9388	9843	38.599	1.28	**98.66**	0.06	98.1	**7**	**24m**	1

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VEGFT-SS207 End of Study SEC analysis
Device 3 and Device 7 (Control Vial) t=0

Export line #	Sample ID	Cal ID	Result ID	Conc	Total Agg (%)	Native (%)	Total Deg (%)	VEGFT Recovered (%)	Device	t=0 Stress	Syringe / rep #
11	03 S207 t=0 D3 r2 set1	9388	9503	39.346	0.79	**99.21**	0.00	99.6	**3**	**t=0**	2.0
12	03 S207 t=0 D3 r3 set1	9388	9502	38.814	0.78	**99.22**	0.00	100.5	**3**	**t=0**	3.0
13	03 S207 t=0 D3 r4 set1	9388	9501	38.371	0.76	**99.24**	0.00	99.0	**3**	**t=0**	4.0
14	03 S207 t=0 D3 r5 set2	9388	9500	41.302	0.77	**99.23**	0.00	99.6	**3**	**t=0**	5.0
3	03 S207 t=0 D3 r2 set1	9388	9730	39.669	0.88	**99.12**	0.00	100.4	**3**	**t=0**	2.0
4	03 S207 t=0 D3 r3 set1	9388	9731	38.39	0.87	**99.13**	0.00	99.5	**3**	**t=0**	3.0
6	03 S207 t=0 D3 r4 set1	9388	9735	39.141	0.86	**99.14**	0.00	101.0	**3**	**t=0**	4.0
7	03 S207 t=0 D3 r5 set2	9388	9736	41.664	0.90	**99.10**	0.00	100.4	**3**	**t=0**	5.0
Avg	*03 S207 t=0 D3 r2 set1*			*39.5075*	*0.84*	***99.17***	*0.00*	*100.0*	***3***	***t=0***	*2.0*
Avg	*03 S207 t=0 D3 r3 set1*			*38.602*	*0.83*	***99.18***	*0.00*	*100.0*	***3***	***t=0***	*3.0*
Avg	*03 S207 t=0 D3 r4 set1*			*38.756*	*0.81*	***99.19***	*0.00*	*100.0*	***3***	***t=0***	*4.0*
Avg	*03 S207 t=0 D3 r5 set2*			*41.483*	*0.84*	***99.17***	*0.00*	*100.0*	***3***	***t=0***	*5.0*
Avg	***VGFT-SS207 t=0 D3***			***39.59***	***0.83***	***99.17***	***0.00***	***100.0***	***3***	***t=0***	***All***
15	03 S207 t=0 D7 r1 set1	9388	9499	41.252	1.00	**99.00**	0.00	105.4	**7**	**t=0**	1.0
16	03 S207 t=0 D7 r2 set1	9388	9498	40.06	0.86	**99.14**	0.00	101.1	**7**	**t=0**	2.0
17	03 S207 t=0 D7 r3 set1	9388	9497	38.901	0.91	**99.09**	0.00	101.2	**7**	**t=0**	3.0
18	03 S207 t=0 D7 r4 set2	9388	9496	39.701	0.52	**99.48**	0.00	98.6	**7**	**t=0**	4.0
8	03 S207 t=0 D7 r1 set1	9388	9737	36.997	1.26	**98.74**	0.00	94.6	**7**	**t=0**	1.0
9	03 S207 t=0 D7 r2 set1	9388	9738	39.189	1.06	**98.94**	0.00	98.9	**7**	**t=0**	2.0
10	03 S207 t=0 D7 r3 set1	9388	9739	37.946	1.04	**98.96**	0.00	98.8	**7**	**t=0**	3.0
11	03 S207 t=0 D7 r4 set2	9388	9740	40.796	0.70	**99.30**	0.00	101.4	**7**	**t=0**	4.0
Avg	*03 S207 t=0 D7 r1 set1*			*39.1245*	*1.13*	***98.87***	*0.00*	*100.0*	***7***	***t=0***	*1.0*
Avg	*03 S207 t=0 D7 r2 set1*			*39.6245*	*0.96*	***99.04***	*0.00*	*100.0*	***7***	***t=0***	*2.0*
Avg	*03 S207 t=0 D7 r3 set1*			*38.4235*	*0.98*	***99.03***	*0.00*	*100.0*	***7***	***t=0***	*3.0*
Avg	*03 S207 t=0 D7 r4 set2*			*40.2485*	*0.61*	***99.39***	*0.00*	*100.0*	***7***	***t=0***	*4.0*
Avg	***VGFT-SS207 t=0 D7***			***39.36***	***0.92***	***99.08***	***0.00***	***100.0***	***7***	***t=0***	***All***

VEGFT-SS207 End of Study SEC analysis
Device 3 and Device 7 (Control Vial) 25C

Export line #	Sample ID	Cal ID	Result ID	Conc	Total Agg (%)	Native (%)	Total Deg (%)	VEGFT Recovered (%)	Device	25ºC Stress (months)	Syringe / rep #
33	03 SS207 25C 0.5m D3 S1	9388	9488	45.448	1.24	**98.76**	0.00	114.8	**3**	**0.5m**	1
34	03 SS207 25C 0.5m D3 S2	9388	9487	38.519	0.93	**99.07**	0.00	97.3	**3**	**0.5m**	2
35	03 SS207 25C 0.5m D3 S3	9388	9486	37.888	0.96	**99.04**	0.00	95.7	**3**	**0.5m**	3
36	03 SS207 25C 0.5m D3 S4	9388	9485	38.393	0.80	**99.20**	0.00	97.0	**3**	**0.5m**	4
	03 SS207 25C 0.5m D3 Avg			**40.1**	**1.0**	**99.0**	**0.0**	**101.2**			
37	03 SS207 25C 0.5m D7 R1	9388	9484	40.341	0.99	**99.01**	0.00	102.5	**7**	**0.5m**	1
38	03 SS207 25C 0.5m D7 R2	9388	9483	38.824	1.01	**98.99**	0.00	98.7	**7**	**0.5m**	2
	03 SS207 25C 0.5m D7 Avg			**39.6**	**1.0**	**99.0**	**0.0**	**100.6**			
39	03 SS207 25C 1m D3 S1	9388	9482	39.574	1.06	**98.91**	0.02	100.0	**3**	**1m**	1
40	03 SS207 25C 1m D3 S2	9388	9481	40.894	1.12	**98.84**	0.04	103.3	**3**	**1m**	2
41	03 SS207 25C 1m D3 S3	9388	9480	38.942	1.06	**98.89**	0.05	98.4	**3**	**1m**	3
42	03 SS207 25C 1m D3 S4	9388	9479	40.349	1.15	**98.82**	0.04	101.9	**3**	**1m**	4
	03 SS207 25C 1m D3 AVG			**39.9**	**1.1**	**98.9**	**0.0**	**100.9**			
43	03 SS207 25C 1m D7 R1	9388	9478	39.069	0.98	**98.96**	0.06	99.3	**7**	**1m**	1
44	03 SS207 25C 1m D7 R2	9388	9477	38.452	1.01	**98.96**	0.03	97.7	**7**	**1m**	2
	03 SS207 25C 1m D7 AVG			**38.8**	**1.0**	**99.0**	**0.0**	**98.5**			
45	03 SS207 25C 2m D3 S1	9388	9476	38.882	1.31	**98.58**	0.12	98.2	**3**	**2m**	1
46	03 SS207 25C 2m D3 S2	9388	9475	39.768	1.41	**98.49**	0.10	100.5	**3**	**2m**	2
47	03 SS207 25C 2m D3 S3	9388	9474	40.197	1.30	**98.62**	0.08	101.5	**3**	**2m**	3
48	03 SS207 25C 2m D3 S4	9388	9473	38.588	1.24	**98.64**	0.12	97.5	**3**	**2m**	4
	03 SS207 25C 2m D3 AVG			**39.4**	**1.3**	**98.6**	**0.1**	**99.4**			
49	03 SS207 25C 2m D7 R1	9388	9472	44.686	1.56	**98.33**	0.11	113.5	**7**	**2m**	1
50	03 SS207 25C 2m D7 R2	9388	9471	39.892	1.39	**98.49**	0.13	101.4	**7**	**2m**	2
	03 SS207 25C 2m D7 AVG			**42.3**	**1.5**	**98.4**	**0.1**	**107.5**			
51	03 SS207 25C 3m D3 S1	9388	9470	38.863	1.49	**98.35**	0.16	98.2	**3**	**3m**	1
52	03 SS207 25C 3m D3 S2	9388	9469	38.73	1.55	**98.28**	0.17	97.8	**3**	**3m**	2
53	03 SS207 25C 3m D3 S3	9388	9468	35.544	1.45	**98.38**	0.17	89.8	**3**	**3m**	3
54	03 SS207 25C 3m D3 S4	9388	9467	39.048	1.51	**98.32**	0.18	98.6	**3**	**3m**	4
	03 SS207 25C 3m D3 AVG			**38.0**	**1.5**	**98.3**	**0.2**	**96.1**			
55	03 SS207 25C 3m D7 R1	9388	9466	40.118	1.43	**98.38**	0.19	101.9	**7**	**3m**	1
56	03 SS207 25C 3m D7 R2	9388	9465	36.976	1.41	**98.40**	0.20	94.0	**7**	**3m**	2
	03 SS207 25C 3m D7 AVG			**38.5**	**1.4**	**98.4**	**0.2**	**97.9**			
57	03 SS207 25C 4m D3 S1	9388	9464	39.809	1.66	**98.12**	0.22	100.6	**3**	**4m**	1
58	03 SS207 25C 4m D3 S2	9388	9463	40.751	1.83	**97.98**	0.20	102.9	**3**	**4m**	2
59	03 SS207 25C 4m D3 S3	9388	9462	41.009	1.71	**98.10**	0.19	103.6	**3**	**4m**	3
60	03 SS207 25C 4m D3 S4	9388	9458	37.94	1.67	**98.10**	0.23	95.8	**3**	**4m**	4
	03 SS207 25C 4m D3 AVG			**39.9**	**1.7**	**98.1**	**0.2**	**100.7**			
61	03 SS207 25C 4m D7 R1	9388	9457	39.898	1.75	**98.01**	0.25	101.4	**7**	**4m**	1
62	03 SS207 25C 4m D7 R2	9388	9456	39.645	1.84	**97.92**	0.24	100.7	**7**	**4m**	2
	03 SS207 25C 4m D7 AVG			**39.8**	**1.8**	**98.0**	**0.2**	**101.1**			
63	03 SS207 25C 5m D3 S1	9388	9455	39.522	1.85	**97.88**	0.27	99.8	**3**	**5m**	1
64	03 SS207 25C 5m D3 S2	9388	9454	40.09	1.95	**97.79**	0.26	101.3	**3**	**5m**	2
65	03 SS207 25C 5m D3 S3	9388	9453	36.115	1.88	**97.83**	0.26	91.2	**3**	**5m**	3
66	03 SS207 25C 5m D3 S4	9388	9452	38.791	1.88	**97.85**	0.26	98.0	**3**	**5m**	4
	03 SS207 25C 5m D3 AVG			**38.6**	**1.9**	**97.8**	**0.3**	**97.6**			
67	03 SS207 25C 5m D7 R1	9388	9451	39.065	1.80	**97.90**	0.30	99.3	**7**	**5m**	1
68	03 SS207 25C 5m D7 R2	9388	9450	37.924	1.73	**97.97**	0.30	96.4	**7**	**5m**	2
	03 SS207 25C 5m D7 AVG			**38.5**	**1.8**	**97.9**	**0.3**	**97.8**			
69	03 SS207 25C 6m D3 S1	9388	9449	38.809	1.98	**97.68**	0.34	98.0	**3**	**6m**	1
70	03 SS207 25C 6m D3 S2	9388	9448	39.202	2.02	**97.62**	0.33	99.0	**3**	**6m**	2
71	03 SS207 25C 6m D3 S3	9388	9447	38.135	2.05	**97.62**	0.33	96.3	**3**	**6m**	3
72	03 SS207 25C 6m D3 S4	9388	9446	38.894	2.08	**97.59**	0.33	98.2	**3**	**6m**	4
	03 SS207 25C 6m D3 AVG			**38.8**	**2.0**	**97.6**	**0.3**	**97.9**			
73	03 SS207 25C 6m D7 R1	9388	9445	39.417	2.14	**97.51**	0.35	100.2	**7**	**6m**	1
23	03 SS207 25C ~~5C~~ 6m D7 R1	9388	9752	38.261	2.08	**97.54**	0.38	97.2	**7**	**6m**	1
Avg	***03 SS207 25C 6m D7 R1***			***38.839***	***2.11***	***97.53***	***0.37***	***98.7***	***7***	***6m***	***1***
74	03 SS207 25C 6m D7 R3	9388	9444	39.126	1.98	**97.64**	0.36	99.4	**7**	**6m**	3
24	03 SS207 25C ~~5C~~ 6m D7 R3	9388	9753	40.077	2.21	**97.41**	0.38	101.8	**7**	**6m**	3
Avg	*03 SS207 25C 6m D7 R3*			*39.6015*	*2.10*	***97.53***	*0.37*	*100.6*	***7***	***6m***	*3*
	03 SS207 25C 6m D7 AVG			***39.2***	***2.1***	***97.5***	***0.4***	***99.7***			

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VEGFT-SS207 End of Study SEC analysis
Device 3 and Device 7 (Control Vial) 37C

Export line #	Sample ID	Cal ID	Result ID	Conc	Total Agg (%)	Native (%)	Total Deg (%)	VEGFT Recovered (%)	Device	37ºC Stress (days)	Syringe / rep #
89	03 SS207 37C 7d D3 S1	9388	9429	38.233	2.22	**97.70**	0.07	96.6	**3**	**7d**	1
90	03 SS207 37C 7d D3 S2	9388	9428	39.065	2.35	**97.55**	0.10	98.7	**3**	**7d**	2
91	03 SS207 37C 7d D3 S3	9388	9427	39.929	2.48	**97.45**	0.07	100.9	**3**	**7d**	3
92	03 SS207 37C 7d D3 S4	9388	9426	39.484	2.47	**97.47**	0.06	99.7	**3**	**7d**	4
	03 SS207 37C 7d D3 AVG			**39.2**	**2.4**	**97.5**	**0.1**	**99.0**			
93	03 SS207 37C 7d D7 R1	9388	9425	39.788	2.42	**97.46**	0.12	101.1	**7**	**7d**	1
94	03 SS207 37C 7d D7 R2	9388	9424	40.342	2.55	**97.37**	0.08	102.5	**7**	**7d**	2
95	03 SS207 37C 7d D7 R3	9388	9423	41.046	2.52	**97.35**	0.12	104.3	**7**	**7d**	3
	03 SS207 37C 7d D7 AVG			**40.4**	**2.5**	**97.4**	**0.1**	**102.6**			
19	03 SS207 37C 14d D3 S1	9388	9495	38.753	3.37	**96.38**	0.16	97.9	**3**	**14d**	1
20	03 SS207 37C 14d D3 S2	9388	9494	39.158	3.51	**96.22**	0.16	98.9	**3**	**14d**	2
21	03 SS207 37C 14d D3 S3	9388	9493	42.8	3.84	**95.76**	0.15	108.1	**3**	**14d**	3
22	03 SS207 37C 14d D3 S4	9388	9492	41.537	4.39	**95.21**	0.15	104.9	**3**	**14d**	4
23	03 SS207 37C 14d D7 R1	9388	9491	44.261	4.56	**94.79**	0.18	112.5	**7**	**14d**	1
24	03 SS207 37C 14d D7 R2	9388	9490	38.877	4.05	**95.60**	0.21	98.8	**7**	**14d**	2
	03 SS207 37C 14d D7 R3										
75	03 SS207 37C 14d D3 S1	9388	9443	38.733	3.50	**96.28**	0.17	97.8	**3**	**14d**	1
96	03 SS207 37C 14d D3 S2	9388	9422	39.437	3.63	**96.13**	0.18	99.6	**3**	**14d**	2
97	03 SS207 37C 14d D3 S3	9388	9421	38.816	3.83	**95.88**	0.16	98.1	**3**	**14d**	3
98	03 SS207 37C 14d D3 S4	9388	9420	39.281	4.27	**95.41**	0.17	99.2	**3**	**14d**	4
99	03 SS207 37C 14d D7 R1	9388	9419	40.812	4.14	**95.49**	0.21	103.7	**7**	**14d**	1
100	03 SS207 37C 14d D7 R2	9388	9418	39.518	4.12	**95.53**	0.23	100.4	**7**	**14d**	2
101	03 SS207 37C 14d D7 R3	9388	9417	38.956	4.24	**95.39**	0.21	99.0	**7**	**14d**	3
Avg	*03 SS207 37C 14d D3 S1*			*38.743*	*3.44*	***96.33***	*0.165*	*97.9*	***3***	***14d***	*1*
Avg	*03 SS207 37C 14d D3 S2*			*39.2975*	*3.57*	***96.175***	*0.17*	*99.3*	***3***	***14d***	*2*
Avg	*03 SS207 37C 14d D3 S3*			*40.808*	*3.835*	***95.82***	*0.155*	*103.1*	***3***	***14d***	*3*
Avg	*03 SS207 37C 14d D3 S4*			*40.409*	*4.33*	***95.31***	*0.16*	*102.1*	***3***	***14d***	*4*
Avg	*03 SS207 37C 14d D7 R1*			*42.5365*	*4.35*	***95.14***	*0.195*	*108.1*	***7***	***14d***	*1*
Avg	*03 SS207 37C 14d D7 R2*			*39.1975*	*4.085*	***95.565***	*0.22*	*99.6*	***7***	***14d***	*2*
	03 SS207 37C 14d D3 AVG			***39.8***	***3.8***	***95.9***	***0.2***	***100.6***			
	03 SS207 37C 14d D7 AVG			***40.9***	***4.2***	***95.4***	***0.2***	***103.8***			
76	03 SS207 37C 21d D3 S1	9388	9442	42.091	4.93	**94.65**	0.15	106.3	**3**	**21d**	1
77	03 SS207 37C 21d D3 S2	9388	9441	39.055	4.70	**94.91**	0.24	98.7	**3**	**21d**	2
78	03 SS207 37C 21d D3 S3	9388	9440	39.102	4.66	**94.92**	0.24	98.8	**3**	**21d**	3
79	03 SS207 37C 21d D3 S4	9388	9439	38.276	5.48	**94.02**	0.25	96.7	**3**	**21d**	4
	03 SS207 37C 21d D3 AVG			**39.6**	**4.9**	**94.6**	**0.2**	**100.1**			
80	03 SS207 37C 21d D7 R1	9388	9438	39.908	5.53	**94.47**	0.00	101.4	**7**	**21d**	1
81	03 SS207 37C 21d D7 R2	9388	9437	38.942	5.70	**93.70**	0.30	98.9	**7**	**21d**	2
82	03 SS207 37C 21d D7 R3	9388	9436	38.906	5.68	**93.72**	0.30	98.9	**7**	**21d**	3
	03 SS207 37C 21d D7 AVG			**39.3**	**5.6**	**94.0**	**0.2**	**99.7**			
83	03 SS207 37C 28d D3 S1	9388	9435	38.128	5.99	**93.38**	0.29	96.3	**3**	**28d**	1
84	03 SS207 37C 28d D3 S2	9388	9434	38.783	6.03	**93.34**	0.31	98.0	**3**	**28d**	2
85	03 SS207 37C 28d D3 S3	9388	9433	39.509	6.76	**92.36**	0.29	99.8	**3**	**28d**	3
	03 SS207 37C 28d D3 AVG			**38.8**	**6.3**	**93.0**	**0.3**	**98.0**			
86	03 SS207 37C 28d D7 R1	9388	9432	40.902	7.12	**92.18**	0.00	103.9	**7**	**28d**	1
87	03 SS207 37C 28d D7 R2	9388	9431	41.126	7.12	**91.88**	0.36	104.5	**7**	**28d**	2
88	03 SS207 37C 28d D7 R3	9388	9430	39.234	7.01	**91.95**	0.35	99.7	**7**	**28d**	3
	03 SS207 37C 28d D7 AVG			**40.4**	**7.1**	**92.0**	**0.2**	**102.7**			

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VEGFT-SS207 End of Study SEC analysis
Device 3 and Device 7 (Control Vial) 5C

Export line #	Sample ID	Cal ID	Result ID	Conc	Total Agg (%)	Native (%)	Total Deg (%)	VEGFT Recovered (%)	Device	5ºC Stress (months)	Syringe / rep #
106	03 SS207 5C 0.5m D3 S1	9388	9540	40.606	0.83	**99.17**	0.00	102.6	**3**	**0.5m**	1
107	03 SS207 5C 0.5m D3 S2	9388	9539	38.254	0.73	**99.23**	0.00	96.6	**3**	**0.5m**	2
108	03 SS207 5C 0.5m D3 S4	9388	9538	39.563	0.69	**99.31**	0.00	99.9	**3**	**0.5m**	4
	03 SS207 5C 0.5m D3 AVG			**39.5**	**0.8**	**99.2**	**0.0**	**99.7**			
109	03 SS207 5C 0.5m D7 R1	9388	9537	41.338	0.77	**99.23**	0.00	105.0	**7**	**0.5m**	1
110	03 SS207 5C 0.5m D7 R2	9388	9536	2.1	1.57	**98.43**	0.00	5.3	**7**	**0.5m**	2
111	03 SS207 5C 0.5m D7 R3	9388	9535	38.394	0.75	**99.22**	0.00	97.6	**7**	**0.5m**	3
	03 SS207 5C 0.5m D7 AVG			**27.3**	**1.0**	**99.0**	**0.0**	**69.3**			
112	03 SS207 5C 1m D3 S1	9388	9534	40.62	1.00	**99.00**	0.00	102.6	**3**	**1m**	1
113	03 SS207 5C 1m D3 S2	9388	9533	39.417	0.87	**99.13**	0.00	99.6	**3**	**1m**	2
114	03 SS207 5C 1m D3 S3	9388	9532	39.188	0.91	**99.09**	0.00	99.0	**3**	**1m**	3
115	03 SS207 5C 1m D3 S4	9388	9531	41.237	0.93	**99.07**	0.00	104.2	**3**	**1m**	4
	03 SS207 5C 1m D3 AVG			**40.1**	**0.9**	**99.1**	**0.0**	**101.3**			
116	03 SS207 5C 1m D7 R1	9388	9530	41.042	0.72	**99.28**	0.00	104.3	**7**	**1m**	1
117	03 SS207 5C 1m D7 R2	9388	9529	38.824	0.71	**99.27**	0.00	98.7	**7**	**1m**	2
118	03 SS207 5C 1m D7 R3	9388	9528	37.721	0.66	**99.32**	0.00	95.8	**7**	**1m**	3
	03 SS207 5C 1m D7 AVG			**39.2**	**0.7**	**99.3**	**0.0**	**99.6**			
120	03 SS207 5C 2m D3 S1	9388	9526	39.56	0.74	**99.26**	0.00	99.9	**3**	**2m**	1
121	03 SS207 5C 2m D3 S2	9388	9525	40.235	0.86	**99.14**	0.00	101.6	**3**	**2m**	2
122	03 SS207 5C 2m D3 S3	9388	9524	40.77	0.88	**99.12**	0.00	103.0	**3**	**2m**	3
123	03 SS207 5C 2m D3 S4	9388	9523	38.753	0.75	**99.25**	0.00	97.9	**3**	**2m**	4
	03 SS207 5C 2m D3 AVG			**39.8**	**0.8**	**99.2**	**0.0**	**100.6**			
124	03 SS207 5C 2m D7 R1	9388	9522	39.837	0.87	**99.13**	0.00	101.2	**7**	**2m**	1
125	03 SS207 5C 2m D7 R2	9388	9521	40.628	0.93	**99.07**	0.00	103.2	**7**	**2m**	2
126	03 SS207 5C 2m D7 R3	9388	9520	40.562	0.93	**99.04**	0.00	103.1	**7**	**2m**	3
	03 SS207 5C 2m D7 AVG			**40.3**	**0.9**	**99.1**	**0.0**	**102.5**			
127	03 SS207 5C 3m D3 S1	9388	9519	42.081	0.93	**99.07**	0.00	106.3	**3**	**3m**	1
128	03 SS207 5C 3m D3 S2	9388	9518	35.75	0.84	**99.16**	0.00	90.3	**3**	**3m**	2
129	03 SS207 5C 3m D3 S3	9388	9517	39.053	0.82	**99.18**	0.00	98.7	**3**	**3m**	3
130	03 SS207 5C 3m D3 S4	9388	9516	39.57	0.76	**99.24**	0.00	100.0	**3**	**3m**	4
	03 SS207 5C 3m D3 AVG			**39.1**	**0.8**	**99.2**	**0.0**	**98.8**			
131	03 SS207 5C 3m D7 R1	9388	9515	40.864	0.69	**99.31**	0.00	103.8	**7**	**3m**	1
132	03 SS207 5C 3m D7 R2	9388	9514	41.244	0.81	**99.19**	0.00	104.8	**7**	**3m**	2
133	03 SS207 5C 3m D7 R3	9388	9513	39.988	0.87	**99.10**	0.00	101.6	**7**	**3m**	3
	03 SS207 5C 3m D7 AVG			**40.7**	**0.8**	**99.2**	**0.0**	**103.4**			
135	03 SS207 5C 4m D3 S1	9388	9511	42.102	0.96	**99.04**	0.00	106.4	**3**	**4m**	1
136	03 SS207 5C 4m D3 S2	9388	9510	40.033	0.87	**99.13**	0.00	101.1	**3**	**4m**	2
137	03 SS207 5C 4m D3 S3	9388	9509	39.699	0.99	**98.99**	0.00	100.3	**3**	**4m**	3
138	03 SS207 5C 4m D3 S4	9388	9508	39.609	0.94	**99.06**	0.00	100.1	**3**	**4m**	4
	03 SS207 5C 4m D3 AVG			**40.4**	**0.9**	**99.1**	**0.0**	**102.0**			
16	03 SS207 5C 4m D7 R1	9388	9846	41.492	3.42	**96.58**	0	105.4	**7**	**4m**	1
17	03 SS207 5C 4m D7 R3	9388	9847	39.046	0.83	**99.17**	0	99.2	**7**	**4m**	3
	03 SS207 5C 4m D7 AVG			**40.3**	**2.1**	**97.9**	**0.0**	**102.3**			
12	03 SS207 5C 5m D3 S1	9388	9741	39.19	0.87	**99.13**	0.00	99.0	**3**	**5m**	1
13	03 SS207 5C 5m D3 S2	9388	9742	40.022	0.79	**99.21**	0.00	101.1	**3**	**5m**	2
14	03 SS207 5C 5m D3 S3	9388	9743	38.735	0.86	**99.14**	0.00	97.8	**3**	**5m**	3
15	03 SS207 5C 5m D3 S4	9388	9744	39.338	0.87	**99.13**	0.00	99.4	**3**	**5m**	4
	03 SS207 5C 5m D3 AVG			**39.3**	**0.8**	**99.2**	**0.0**	**99.3**			
16	03 SS207 5C 5m D7 R1	9388	9745	40.123	1.04	**98.96**	0.00	102.0	**7**	**5m**	1
17	03 SS207 5C 5m D7 R3	9388	9746	39.215	0.87	**99.13**	0.00	99.6	**7**	**5m**	3
	03 SS207 5C 5m D7 AVG			**39.7**	**1.0**	**99.0**	**0.0**	**100.8**			
19	03 SS207 5C 6m D3 S1	9388	9748	37.852	1.00	**99.00**	0.00	95.6	**3**	**6m**	1
20	03 SS207 5C 6m D3 S2	9388	9749	39.365	0.88	**99.12**	0.00	99.4	**3**	**6m**	2
21	03 SS207 5C 6m D3 S3	9388	9750	39.233	0.92	**99.08**	0.00	99.1	**3**	**6m**	3
22	03 SS207 5C 6m D3 S4	9388	9751	39.321	0.92	**99.08**	0.00	99.3	**3**	**6m**	4
	03 SS207 5C 6m D3 AVG			**38.9**	**0.9**	**99.1**	**0.0**	**98.4**			
104	03 SS207 ~~25C~~ 5C 6m D7 R1	9388	9542	41.301	0.92	**99.08**	0.00	104.9	**7**	**6m**	1
105	03 SS207 ~~25C~~ 5C 6m D7 R2	9388	9541	40.768	0.83	**99.17**	0.00	103.6	**7**	**6m**	2
	03 SS207 ~~25C~~ 5C 6m D7 AVG			**41.0**	**0.9**	**99.1**	**0.0**	**104.3**			
25	03 SS207 5C 9m D3 S1	9388	9754	46.837	1.42	**98.58**	0.00	118.3	**3**	**9m**	1
26	03 SS207 5C 9m D3 S2	9388	9755	39.293	0.99	**99.01**	0.00	99.3	**3**	**9m**	2
27	03 SS207 5C 9m D3 S3	9388	9756	39.777	1.20	**98.80**	0.00	100.5	**3**	**9m**	3
28	03 SS207 5C 9m D3 S4	9388	9757	39.355	1.05	**98.93**	0.02	99.4	**3**	**9m**	4
	03 SS207 5C 9m D3 AVG			**41.3**	**1.2**	**98.8**	**0.0**	**104.4**			
29	03 SS207 5C 9m D7 R1	9388	9758	39.84	0.96	**99.02**	0.02	101.2	**7**	**9m**	1
30	03 SS207 5C 9m D7 R3	9388	9759	40.346	0.94	**99.06**	0.00	102.5	**7**	**9m**	3
	03 SS207 5C 9m D7 AVG			**40.1**	**1.0**	**99.0**	**0.0**	**101.9**			
34	03 SS207 5C 12m D3 S1	9388	9763	41.094	1.25	**98.74**	0.01	103.8	**3**	**12m**	1
35	03 SS207 5C 12m D3 S2	9388	9764	38.321	0.99	**99.01**	0.00	96.8	**3**	**12m**	2
36	03 SS207 5C 12m D3 S3	9388	9765	39.079	0.97	**99.01**	0.02	98.7	**3**	**12m**	3
37	03 SS207 5C 12m D3 S4	9388	9766	38.768	0.98	**98.98**	0.04	97.9	**3**	**12m**	4

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	03 SS207 5C 12m D3 AVG			**39.3**	**1.0**	**98.9**	**0.0**	**99.3**			
38	03 SS207 5C 12m D7 R1	9388	9767	39.699	0.93	**99.03**	0.04	100.9	**7**	**12m**	1
	03 SS207 5C 12m D7 AVG			**39.7**	**0.9**	**99.0**	**0.0**	**100.9**			
9	03 SS207 5C 15m D3 S1	9388	9830	37.542	1.14	**98.82**	0.05	94.8	**3**	**15m**	1
1	03 SS207 5C 15m D3 S2	9388	9831	38.672	1.09	**98.87**	0.04	97.7	**3**	**15m**	2
2	03 SS207 5C 15m D3 S3	9388	9832	39.16	1.09	**98.87**	0.05	98.9	**3**	**15m**	3
3	03 SS207 5C 15m D3 S4	9388	9833	38.097	1.06	**98.9**	0.04	96.2	**3**	**15m**	4
	03 SS207 5C 15m D3 AVG			**38.4**	**1.1**	**98.9**	**0.0**	**96.9**			
4	03 SS207 5C 15m D7 R1	9388	9834	46.635	1.57	**98.4**	0.04	118.5	**7**	**15m**	1
5	03 SS207 5C 15m D7 R2	9388	9835	40.645	1.12	**98.86**	0.02	103.3	**7**	**15m**	2
	03 SS207 5C 15m D7 AVG			**43.6**	**1.3**	**98.6**	**0.0**	**110.9**			
6	03 SS207 5C 18m D3 S1	9388	9836	37.988	1.15	**98.79**	0.05	96.0	**3**	**18m**	1
8	03 SS207 5C 18m D3 S2	9388	9837	38.31	1.11	**98.84**	0.05	96.8	**3**	**18m**	2
10	03 SS207 5C 18m D3 S3	9388	9838	38.824	1.13	**98.82**	0.05	98.1	**3**	**18m**	3
11	03 SS207 5C 18m D3 S4	9388	9839	39.351	1.1	**98.82**	0.08	99.4	**3**	**18m**	4
	03 SS207 5C 18m D3 AVG			**38.6**	**1.1**	**98.8**	**0.1**	**97.6**			
12	03 SS207 5C 18m D7 R1	9388	9840	40.023	1.29	**98.64**	0.07	101.7	**7**	**18m**	1
	03 SS207 5C 18m D7 AVG			**40.0**	**1.3**	**98.6**	**0.1**	**101.7**			
13	03 SS207 5C 24m D3 S1	9388	9841	40.579	1.32	**98.59**	0.09	102.5	**3**	**24m**	1
14	03 SS207 5C 24m D3 S4	9388	9842	39.003	1.29	**98.64**	0.06	98.5	**3**	**24m**	4
	03 SS207 5C 24m D3 AVG			**39.8**	**1.3**	**98.6**	**0.1**	**100.5**			
15	03 SS207 5C 24m D7 R1	9388	9843	38.599	1.28	**98.66**	0.06	98.1	**7**	**24m**	1
	03 SS207 5C 24m D7 AVG			**38.6**	**1.3**	**98.7**	**0.1**	**98.1**			

Component Summary For % Area

#	Sample Name	Inj	Agg 3	Total Agg	Total VEGFT	Agg 2	Agg 1	Native	Total Deg	Deg 1	Deg 2	Deg 3	
					Total VEGFT			**Total Agg**	**Native**	**total deg**			
1	WFI	1		3.54	100	3.54			**22.98**	73.48			
2	WFI	1	18.18	51.29	100	3.32	7.06	2.80	**21.32**	27.39	27.39		
3	03 EF-7630-13 10mg/mL 10ug	1		3.11	100		0.41	2.70	**96.89**				
4	03 EF-7630-13 10mg/mL 15ug	1		2.28	100			2.28	**97.72**				
5	03 EF-7630-13 10mg/mL 20ug	1		2.31	100			2.31	**97.69**				
6	03 EF-7630-13 10mg/mL 20ug	2		2.32	100			2.32	**97.68**				
7	03 EF-7630-13 10mg/mL 20ug	3		2.32	100			2.32	**97.68**				
8	03 EF-7630-13 10mg/mL 20ug	4		2.33	100			2.33	**97.67**				
9	03 EF-7630-13 10mg/mL 25ug	1		2.34	100		0.01	2.34	**97.66**				
10	03 EF-7630-13 10mg/mL 30ug	1		2.34	100	0.01		2.33	**97.66**				
11	03 S207 t=0 D3 r2 set1	1		0.79	100			0.79	**99.21**				
12	03 S207 t=0 D3 r3 set1	1		0.78	100			0.78	**99.22**				
13	03 S207 t=0 D3 r4 set1	1		0.76	100			0.76	**99.24**				
14	03 S207 t=0 D3 r5 set2	1		0.77	100			0.77	**99.23**				
15	03 S207 t=0 D7 r1 set1	1		1	100			1.00	**99.00**				
16	03 S207 t=0 D7 r2 set1	1		0.86	100			0.86	**99.14**				
17	03 S207 t=0 D7 r3 set1	1		0.91	100			0.91	**99.09**				
18	03 S207 t=0 D7 r4 set2	1		0.52	100			0.52	**99.48**				
19	03 SS207 37C 14d D3 S1	1		3.46	100	0.1		3.37	**96.38**	0.16	0.05	0.07	0.03
20	03 SS207 37C 14d D3 S2	1		3.62	100	0.11		3.51	**96.22**	0.16	0.05	0.08	0.03
21	03 SS207 37C 14d D3 S3	1		4.09	100	0.21	0.04	3.84	**95.76**	0.15	0.05	0.07	0.03
22	03 SS207 37C 14d D3 S4	1		4.63	100	0.01	0.01	4.39	**95.21**	0.15	0.05	0.07	0.02
23	03 SS207 37C 14d D7 R1	1		5.03	100	0.41	0.06	4.56	**94.79**	0.18	0.04	0.1	0.03
24	03 SS207 37C 14d D7 R2	1		4.19	100	0.14		4.05	**95.60**	0.21	0.05	0.12	0.04
25	03 EF-7630-13 10mg/mL 10ug	1		3.7	100	1.23		2.47	**96.30**				
26	03 EF-7630-13 10mg/mL 15ug	1		2.03	100			2.03	**97.97**				
27	03 EF-7630-13 10mg/mL 20ug	1		2.15	100			2.15	**97.85**				
28	03 EF-7630-13 10mg/mL 20ug	2		2.21	100	0.01		2.20	**97.79**				
29	03 EF-7630-13 10mg/mL 20ug	3		2.21	100	0.02		2.19	**97.79**				
30	03 EF-7630-13 10mg/mL 20ug	4		2.19	100			2.19	**97.81**				
31	03 EF-7630-13 10mg/mL 25ug	1		2.24	100	0.02	0.01	2.21	**97.76**				
32	03 EF-7630-13 10mg/mL 30ug	1		2.25	100	0.02	0.01	2.22	**97.75**				
33	03 SS207 25C 0.5m D3 S1	1		1.24	100			1.24	**98.76**				
34	03 SS207 25C 0.5m D3 S2	1		0.93	100			0.93	**99.07**				
35	03 SS207 25C 0.5m D3 S3	1		0.96	100			0.96	**99.04**				
36	03 SS207 25C 0.5m D3 S4	1		0.8	100			0.80	**99.20**				
37	03 SS207 25C 0.5m D7 R1	1		0.99	100			0.99	**99.01**				
38	03 SS207 25C 0.5m D7 R2	1		1.01	100			1.01	**98.99**				
39	03 SS207 25C 1m D3 S1	1		1.06	100			1.06	**98.91**	0.02		0.02	
40	03 SS207 25C 1m D3 S2	1		1.12	100	0.01		1.12	**98.84**	0.04	0.01	0.02	
41	03 SS207 25C 1m D3 S3	1		1.06	100	0.01		1.06	**98.89**	0.05	0.01	0.02	
42	03 SS207 25C 1m D3 S4	1		1.15	100			1.15	**98.82**	0.04	0.02	0.02	
43	03 SS207 25C 1m D7 R1	1		0.98	100			0.98	**98.96**	0.06	0.02	0.04	
44	03 SS207 25C 1m D7 R2	1		1.01	100			1.01	**98.96**	0.03		0.03	
45	03 SS207 25C 2m D3 S1	1		1.31	100			1.31	**98.58**	0.12	0.04	0.05	0.02
46	03 SS207 25C 2m D3 S2	1		1.41	100	0.02		1.41	**98.49**	0.10	0.02	0.04	0.02
47	03 SS207 25C 2m D3 S3	1		1.3	100			1.30	**98.62**	0.08	0.04	0.04	
48	03 SS207 25C 2m D3 S4	1		1.24	100			1.24	**98.64**	0.12	0.04	0.05	0.03
49	03 SS207 25C 2m D7 R1	1		1.56	100			1.56	**98.33**	0.11	0.03	0.06	0.02
50	03 SS207 25C 2m D7 R2	1		1.39	100			1.39	**98.49**	0.13	0.04	0.06	0.03
51	03 SS207 25C 3m D3 S1	1		1.49	100			1.49	**98.35**	0.16	0.06	0.07	0.03
52	03 SS207 25C 3m D3 S2	1		1.55	100			1.55	**98.28**	0.17	0.06	0.07	0.04
53	03 SS207 25C 3m D3 S3	1		1.45	100			1.45	**98.38**	0.17	0.06	0.07	0.04
54	03 SS207 25C 3m D3 S4	1		1.51	100			1.51	**98.32**	0.18	0.06	0.07	0.04
55	03 SS207 25C 3m D7 R1	1		1.43	100			1.43	**98.38**	0.19	0.06	0.09	0.04
56	03 SS207 25C 3m D7 R2	1		1.41	100			1.41	**98.40**	0.20	0.06	0.09	0.04
57	03 SS207 25C 4m D3 S1	1		1.66	100			1.66	**98.12**	0.22	0.08	0.1	0.05
58	03 SS207 25C 4m D3 S2	1		1.83	100			1.83	**97.98**	0.20	0.08	0.08	0.04
59	03 SS207 25C 4m D3 S3	1		1.71	100			1.71	**98.10**	0.19	0.07	0.08	0.04
60	03 SS207 25C 4m D3 S4	1		1.67	100			1.67	**98.10**	0.23	0.08	0.09	0.05
61	03 SS207 25C 4m D7 R1	1		1.75	100			1.75	**98.01**	0.25	0.08	0.11	0.05
62	03 SS207 25C 4m D7 R2	1		1.84	100			1.84	**97.92**	0.24	0.07	0.11	0.06
63	03 SS207 25C 5m D3 S1	1		1.85	100			1.85	**97.88**	0.27	0.1	0.12	0.05
64	03 SS207 25C 5m D3 S2	1		1.95	100			1.95	**97.79**	0.26	0.1	0.11	0.06
65	03 SS207 25C 5m D3 S3	1		1.91	100	0.03		1.88	**97.83**	0.26	0.1	0.11	0.05
66	03 SS207 25C 5m D3 S4	1		1.88	100			1.88	**97.85**	0.26	0.1	0.11	0.06
67	03 SS207 25C 5m D7 R1	1		1.8	100			1.80	**97.90**	0.30	0.09	0.14	0.06
68	03 SS207 25C 5m D7 R2	1		1.73	100			1.73	**97.97**	0.30	0.1	0.14	0.06
69	03 SS207 25C 6m D3 S1	1		1.98	100			**1.98**	**97.68**	**0.34**	0.12	0.14	0.08
70	03 SS207 25C 6m D3 S2	1		2.04	100	0.02		**2.02**	**97.62**	**0.33**	0.12	0.14	0.07
71	03 SS207 25C 6m D3 S3	1		2.05	100			**2.05**	**97.62**	**0.33**	0.12	0.14	0.07
72	03 SS207 25C 6m D3 S4	1		2.08	100			**2.08**	**97.59**	**0.33**	0.12	0.14	0.07
73	03 SS207 25C 6m D7 R1	1		2.14	100			**2.14**	**97.51**	**0.35**	0.12	0.17	0.07
74	03 SS207 25C 6m D7 R2	1		2	100	0.02		**1.98**	**97.64**	**0.36**	0.11	0.17	0.08
75	03 SS207 37C 14d D3 S1	1		3.55	100	0.05		3.50	**96.28**	0.17	0.05	0.08	0.04
76	03 SS207 37C 21d D3 S1	1		5.19	100	0.25	0.01	4.93	**94.65**	0.15	0.08	0.06	0.02
77	03 SS207 37C 21d D3 S2	1		4.85	100	0.15		4.70	**94.91**	0.24	0.08	0.11	0.05
78	03 SS207 37C 21d D3 S3	1		4.84	100	0.18		4.66	**94.92**	0.24	0.08	0.11	0.06
79	03 SS207 37C 21d D3 S4	1		5.74	100	0.26		5.48	**94.02**	0.25	0.09	0.11	0.05
80	03 SS207 37C 21d D7 R1	1		5.53	100			5.53	**94.47**				
81	03 SS207 37C 21d D7 R2	1		5.99	100	0.29		5.70	**93.70**	0.30	0.08	0.15	0.07
82	03 SS207 37C 21d D7 R3	1		5.98	100	0.3		5.68	**93.72**	0.30	0.08	0.16	0.06
83	03 SS207 37C 28d D3 S1	1		6.32	100	0.32	0.01	5.99	**93.38**	0.29	0.1	0.13	0.06
84	03 SS207 37C 28d D3 S2	1		6.36	100	0.33		6.03	**93.34**	0.31	0.11	0.14	0.06
85	03 SS207 37C 28d D3 S3	1		7.35	100	0.01	0.11	6.76	**92.36**	0.29	0.1	0.13	0.06
86	03 SS207 37C 28d D7 R1	1		7.82	100	0.6	0.1	7.12	**92.18**				
87	03 SS207 37C 28d D7 R2	1		7.76	100	0.59	0.05	7.12	**91.88**	0.36	0.1	0.18	0.08
88	03 SS207 37C 28d D7 R3	1		7.7	100	0.56	0.12	7.01	**91.95**	0.35	0.1	0.18	0.07
89	03 SS207 37C 7d D3 S1	1		2.22	100			2.22	**97.70**	0.07	0.03	0.04	
90	03 SS207 37C 7d D3 S2	1		2.35	100			2.35	**97.55**	0.10	0.03	0.05	0.02
91	03 SS207 37C 7d D3 S3	1		2.48	100			2.48	**97.45**	0.07	0.03	0.04	

92	03 SS207 37C 7d D3 S4	1		2.47	100			2.47	**97.47**	0.06	0.03	0.03	
93	03 SS207 37C 7d D7 R1	1		2.42	100			2.42	**97.46**	0.12	0.03	0.09	
94	03 SS207 37C 7d D7 R2	1		2.55	100			2.55	**97.37**	0.08	0.03	0.05	
95	03 SS207 37C 7d D7 R3	1		2.53	100	0.01		2.52	**97.35**	0.12	0.01	0.08	0.01
96	03 SS207 37C 14d D3 S2	1		3.7	100	0.07		3.63	**96.13**	0.18	0.05	0.08	0.04
97	03 SS207 37C 14d D3 S3	1		3.96	100	0.1	0.03	3.83	**95.88**	0.16	0.05	0.08	0.03
98	03 SS207 37C 14d D3 S4	1		4.42	100	0.13	0.01	4.27	**95.41**	0.17	0.06	0.08	0.04
99	03 SS207 37C 14d D7 R1	1		4.3	100	0.13	0.04	4.14	**95.49**	0.21	0.06	0.15	
100	03 SS207 37C 14d D7 R2	1		4.24	100	0.12		4.12	**95.53**	0.23	0.06	0.11	0.05
101	03 SS207 37C 14d D7 R3	1		4.39	100	0.13	0.02	4.24	**95.39**	0.21	0.06	0.11	0.05
102	WFI	1			100				**100.00**				
103	03 EF-7630-13 10mg/mL 20ug	1		2.16	100			2.16	**97.84**				
~~104~~	~~03 SS207 25C 6m D7 R1~~	~~1~~	-	~~0.92~~	~~100~~	-	-	~~0.92~~	~~**99.08**~~	-			
~~105~~	~~03 SS207 25C 6m D7 R2~~	~~1~~	-	~~0.83~~	~~100~~	-	-	~~0.83~~	~~**99.17**~~	-			
106	03 SS207 5C 0.5m D3 S1	1		0.83	100			0.83	**99.17**				
107	03 SS207 5C 0.5m D3 S2	1		0.77	100	0.04		0.73	**99.23**				
108	03 SS207 5C 0.5m D3 S4	1		0.69	100			0.69	**99.31**				
109	03 SS207 5C 0.5m D7 R1	1		0.77	100			0.77	**99.23**				
110	03 SS207 5C 0.5m D7 R2	1		1.57	100			1.57	**98.43**				
111	03 SS207 5C 0.5m D7 R3	1		0.78	100	0.01		0.75	**99.22**				
112	03 SS207 5C 1m D3 S1	1		1	100			1.00	**99.00**				
113	03 SS207 5C 1m D3 S2	1		0.87	100			0.87	**99.13**				
114	03 SS207 5C 1m D3 S3	1		0.91	100			0.91	**99.09**				
115	03 SS207 5C 1m D3 S4	1		0.93	100			0.93	**99.07**				
116	03 SS207 5C 1m D7 R1	1		0.72	100			0.72	**99.28**				
117	03 SS207 5C 1m D7 R2	1		0.73	100	0.02		0.71	**99.27**				
118	03 SS207 5C 1m D7 R3	1		0.68	100	0.02		0.66	**99.32**				
119	03 EF-7630-13 10mg/mL 20ug	1		2.14	100			2.14	**97.86**				
120	03 SS207 5C 2m D3 S1	1		0.74	100			0.74	**99.26**				
121	03 SS207 5C 2m D3 S2	1		0.86	100			0.86	**99.14**				
122	03 SS207 5C 2m D3 S3	1		0.88	100			0.88	**99.12**				
123	03 SS207 5C 2m D3 S4	1		0.75	100			0.75	**99.25**				
124	03 SS207 5C 2m D7 R1	1		0.87	100			0.87	**99.13**				
125	03 SS207 5C 2m D7 R2	1		0.93	100			0.93	**99.07**				
126	03 SS207 5C 2m D7 R3	1		0.96	100	0.02		0.93	**99.04**				
127	03 SS207 5C 3m D3 S1	1		0.93	100			0.93	**99.07**				
128	03 SS207 5C 3m D3 S2	1		0.84	100			0.84	**99.16**				
129	03 SS207 5C 3m D3 S3	1		0.82	100			0.82	**99.18**				
130	03 SS207 5C 3m D3 S4	1		0.76	100			0.76	**99.24**				
131	03 SS207 5C 3m D7 R1	1		0.69	100			0.69	**99.31**				
132	03 SS207 5C 3m D7 R2	1		0.81	100			0.81	**99.19**				
133	03 SS207 5C 3m D7 R3	1		0.9	100	0.02		0.87	**99.10**				
134	03 EF-7630-13 10mg/mL 20ug	1		1.94	100			1.94	**98.06**				
135	03 SS207 5C 4m D3 S1	1		0.96	100			0.96	**99.04**				
136	03 SS207 5C 4m D3 S2	1		0.87	100			0.87	**99.13**				
137	03 SS207 5C 4m D3 S3	1		1.01	100	0.02		0.99	**98.99**				
138	03 SS207 5C 4m D3 S4	1		0.94	100			0.94	**99.06**				
139	03 SS207 5C 4m D7 R3	1		51.71	100	1.24			**48.04**	0.25		0.01	0.05

080220 Max Processing export part 2

Component Summary Export2

Component Summary For Area

#	Sample Name	Inj	Total Agg	Total VEGFT	Agg 2	Agg 1	Native	Deg 1	Total Deg	Deg 2	Deg 3	
1	03 SS207 5C 4m D7 R3	1	1888100	78939400	152652267			73332636		380231	12444	73407
2	03 SS207 5C 4m D7 R3	1	76582910	78939400	152652267			73332636		380231	12444	73407
3	03 S207 t=0 D3 r2 set1	1		658120	74938128		658120	74280008				
4	03 S207 t=0 D3 r3 set1	1		634189	72585470		634189	71951281				
5	03 EF-7630-13 10mg/mL 20ug	1	14752	1653724	74992097		1638972	73338373				
6	03 S207 t=0 D3 r4 set1	1		637827	73967116		637827	73329288				
7	03 S207 t=0 D3 r5 set2	1		707989	78607953		707989	77899964				
8	03 S207 t=0 D7 r1 set1	1		879038	70023012		879038	69143974				
9	03 S207 t=0 D7 r2 set1	1	18720	783587	74054177		764867	73270590				
10	03 S207 t=0 D7 r3 set1	1	15250	749379	71768499		734128	71019120				
11	03 S207 t=0 D7 r4 set2	1		538840	77010635		538840	76471795				
12	03 SS207 5C 5m D3 S1	1		642700	74057255		642700	73414555				
13	03 SS207 5C 5m D3 S2	1		598690	75587272		598690	74988582				
14	03 SS207 5C 5m D3 S3	1		627750	73219335		627750	72591585				
15	03 SS207 5C 5m D3 S4	1		645969	74329020		645969	73683050				
16	03 SS207 5C 5m D7 R1	1		789963	75773660		789963	74983697				
17	03 SS207 5C 5m D7 R3	1		644807	74103518		644807	73458711				
18	03 EF-7630-13 10mg/mL 20ug	1	10380	1614188	74650387		1598398	73036200				
19	03 SS207 5C 6m D3 S1	1		713483	71596077		713483	70882595				
20	03 SS207 5C 6m D3 S2	1		653671	74378135		653671	73724464				
21	03 SS207 5C 6m D3 S3	1	11371	684373	74135460		673002	73451087				
22	03 SS207 5C 6m D3 S4	1		682680	74298406		682680	73615726				
23	03 SS207 5C 6m D7 R1	1	17243	1504204	72347282		1486961	70566864	90083	276214	127052	59080
24	03 SS207 5C 6m D7 R3	1		1669145	75688936		1669145	73731222	92534	288569	131371	64664
25	03 SS207 5C 9m D3 S1	1	27712	1252224	88122442	8324	1216188	86870218				
26	03 SS207 5C 9m D3 S2	1		733454	74247263		733454	73513810				
27	03 SS207 5C 9m D3 S3	1	15912	898347	75135905		882434	74237559				
28	03 SS207 5C 9m D3 S4	1	15140	778763	74360416		763623	73566606	15047	15047		
29	03 SS207 5C 9m D7 R1	1		723013	75252904		723013	74517653		12238	12238	
30	03 SS207 5C 9m D7 R3	1	21367	712643	76183280		691275	75470637				
31	VGTO -S258 Syr 2 25C B	1		784722	30529476		784722	29744754				
32	03 EF-7630-13 10mg/mL 20ug	1	5015	1640446	74920526		1603125	73280081				
33	WFI	1			27672			27672				
34	03 SS207 5C 12m D3 S1	1		969120	77559983	4641	964479	76579382		11481	11481	
35	03 SS207 5C 12m D3 S2	1		718824	72458758		718824	71739935				
36	03 SS207 5C 12m D3 S3	1		714508	73852267		714508	73121744	16014	16014		
37	03 SS207 5C 12m D3 S4	1	7637	717609	73281241		717609	72535296	9598	28335	11100	
38	03 SS207 5C 12m D7 R1	1	12230	700202	74992584		700202	74263039	5171	29343	11942	

Component Summary For Amount

#	Sample Name	Inj	Total Agg	Total VEGFT	Total Deg
1	03 SS207 5C 4m D7 R3	1		40.96	
2	03 SS207 5C 4m D7 R3	1		40.96	
3	03 S207 t=0 D3 r2 set1	1		19.835	
4	03 S207 t=0 D3 r3 set1	1		19.195	
5	03 EF-7630-13 10mg/mL 20ug	1		19.849	
6	03 S207 t=0 D3 r4 set1	1		19.571	
7	03 S207 t=0 D3 r5 set2	1		20.832	
8	03 S207 t=0 D7 r1 set1	1		18.498	
9	03 S207 t=0 D7 r2 set1	1		19.594	
10	03 S207 t=0 D7 r3 set1	1		18.973	
11	03 S207 t=0 D7 r4 set2	1		20.398	
12	03 SS207 5C 5m D3 S1	1		19.595	
13	03 SS207 5C 5m D3 S2	1		20.011	
14	03 SS207 5C 5m D3 S3	1		19.367	
15	03 SS207 5C 5m D3 S4	1		19.669	
16	03 SS207 5C 5m D7 R1	1		20.062	
17	03 SS207 5C 5m D7 R3	1		19.608	
18	03 EF-7630-13 10mg/mL 20ug	1		19.756	
19	03 SS207 5C 6m D3 S1	1		18.926	
20	03 SS207 5C 6m D3 S2	1		19.682	
21	03 SS207 5C 6m D3 S3	1		19.616	
22	03 SS207 5C 6m D3 S4	1		19.661	
23	03 SS207 5C 6m D7 R1	1		19.13	
24	03 SS207 5C 6m D7 R3	1		20.039	
25	03 SS207 5C 9m D3 S1	1		23.418	
26	03 SS207 5C 9m D3 S2	1		19.647	
27	03 SS207 5C 9m D3 S3	1		19.888	
28	03 SS207 5C 9m D3 S4	1		19.678	
29	03 SS207 5C 9m D7 R1	1		19.92	
30	03 SS207 5C 9m D7 R3	1		20.173	
31	VGTO -S258 Syr 2 25C B	1		7.763	
32	03 EF-7630-13 10mg/mL 20ug	1		19.83	
33	WFI	1			
34	03 SS207 5C 12m D3 S1	1		20.547	
35	03 SS207 5C 12m D3 S2	1		19.161	
36	03 SS207 5C 12m D3 S3	1		19.539	
37	03 SS207 5C 12m D3 S4	1		19.384	
38	03 SS207 5C 12m D7 R1	1		19.849	

Component Summary For Concentration **080220 Max Processing export part 2**

#	Sample Name	Inj	Calibration Id	Result Id	Cal Curve Id	Total Agg	Total VEGFT	Total Deg
1	03 SS207 5C 4m D7 R3	1	**9388**	9732	9391		81.919	
2	03 SS207 5C 4m D7 R3	1	**9388**	9729	9390		81.919	
3	03 S207 t=0 D3 r2 set1	1	**9388**	9730	9390		39.669	
4	03 S207 t=0 D3 r3 set1	1	**9388**	9731	9390		38.39	
5	03 EF-7630-13 10mg/mL 20ug	1	**9388**	9733	9390		9.925	
6	03 S207 t=0 D3 r4 set1	1	**9388**	9735	9390		39.141	
7	03 S207 t=0 D3 r5 set2	1	**9388**	9736	9390		41.664	
8	03 S207 t=0 D7 r1 set1	1	**9388**	9737	9390		36.997	
9	03 S207 t=0 D7 r2 set1	1	**9388**	9738	9390		39.189	
10	03 S207 t=0 D7 r3 set1	1	**9388**	9739	9390		37.946	
11	03 S207 t=0 D7 r4 set2	1	**9388**	9740	9390		40.796	
12	03 SS207 5C 5m D3 S1	1	**9388**	9741	9390		39.19	
13	03 SS207 5C 5m D3 S2	1	**9388**	9742	9390		40.022	
14	03 SS207 5C 5m D3 S3	1	**9388**	9743	9391		38.735	
15	03 SS207 5C 5m D3 S4	1	**9388**	9744	9390		39.338	
16	03 SS207 5C 5m D7 R1	1	**9388**	9745	9390		40.123	
17	03 SS207 5C 5m D7 R3	1	**9388**	9746	9390		39.215	
18	03 EF-7630-13 10mg/mL 20ug	1	**9388**	9747	9390		9.878	
19	03 SS207 5C 6m D3 S1	1	**9388**	9748	9390		37.852	
20	03 SS207 5C 6m D3 S2	1	**9388**	9749	9390		39.365	
21	03 SS207 5C 6m D3 S3	1	**9388**	9750	9390		39.233	
22	03 SS207 5C 6m D3 S4	1	**9388**	9751	9390		39.321	
23	03 SS207 5C 6m D7 R1	1	**9388**	9752	9390		38.261	
24	03 SS207 5C 6m D7 R3	1	**9388**	9753	9390		40.077	
25	03 SS207 5C 9m D3 S1	1	**9388**	9754	9390		46.837	
26	03 SS207 5C 9m D3 S2	1	**9388**	9755	9390		39.293	
27	03 SS207 5C 9m D3 S3	1	**9388**	9756	9390		39.777	
28	03 SS207 5C 9m D3 S4	1	**9388**	9757	9390		39.355	
29	03 SS207 5C 9m D7 R1	1	**9388**	9758	9390		39.84	
30	03 SS207 5C 9m D7 R3	1	**9388**	9759	9390		40.346	
31	VGTO -S258 Syr 2 25C B	1	**9388**	9760	9390		0.078	
32	03 EF-7630-13 10mg/mL 20ug	1	**9388**	9761	9390		9.915	
33	WFI	1	**9388**	9762	9391			
34	03 SS207 5C 12m D3 S1	1	**9388**	9763	9390		41.094	
35	03 SS207 5C 12m D3 S2	1	**9388**	9764	9390		38.321	
36	03 SS207 5C 12m D3 S3	1	**9388**	9765	9390		39.079	
37	03 SS207 5C 12m D3 S4	1	**9388**	9766	9390		38.768	
38	03 SS207 5C 12m D7 R1	1	**9388**	9767	9390		39.699	

Component Summary For % Area **080220 Max Processing export part 2**

#	Sample Name	Inj	Total Agg	Total VEGFT	Agg 2	Agg 1	Native	Deg 1	Total Deg	Deg 2	Deg 3	
				TotalAgg				**Native**		**total Deg**		
1	03 SS207 5C 4m D7 R3	1	1.24	51.71	100.00			48.04		0.25	0.01	0.05
2	03 SS207 5C 4m D7 R3	1	50.17	51.71	100.00			48.04		0.25	0.01	0.05
3	03 S207 t=0 D3 r2 set1	1		0.88	100.00		0.88	99.12				
4	03 S207 t=0 D3 r3 set1	1		0.87	100.00		0.87	99.13				
5	03 EF-7630-13 10mg/mL 20ug	1	0.02	2.21	100.00		2.19	97.79				
6	03 S207 t=0 D3 r4 set1	1		0.86	100.00		0.86	99.14				
7	03 S207 t=0 D3 r5 set2	1		0.90	100.00		0.90	99.10				
8	03 S207 t=0 D7 r1 set1	1		1.26	100.00		1.26	98.74				
9	03 S207 t=0 D7 r2 set1	1	0.03	1.06	100.00		1.03	98.94				
10	03 S207 t=0 D7 r3 set1	1	0.02	1.04	100.00		1.02	98.96				
11	03 S207 t=0 D7 r4 set2	1		0.70	100.00		0.70	99.30				
12	03 SS207 5C 5m D3 S1	1		0.87	100.00		0.87	99.13				
13	03 SS207 5C 5m D3 S2	1		0.79	100.00		0.79	99.21				
14	03 SS207 5C 5m D3 S3	1		0.86	100.00		0.86	99.14				
15	03 SS207 5C 5m D3 S4	1		0.87	100.00		0.87	99.13				
16	03 SS207 5C 5m D7 R1	1		1.04	100.00		1.04	98.96				
17	03 SS207 5C 5m D7 R3	1		0.87	100.00		0.87	99.13				
18	03 EF-7630-13 10mg/mL 20ug	1	0.01	2.16	100.00		2.14	97.84				
19	03 SS207 5C 6m D3 S1	1		1.00	100.00		1.00	99.00				
20	03 SS207 5C 6m D3 S2	1		0.88	100.00		0.88	99.12				
21	03 SS207 5C 6m D3 S3	1	0.02	0.92	100.00		0.91	99.08				
22	03 SS207 5C 6m D3 S4	1		0.92	100.00		0.92	99.08				
23	03 SS207 5C 6m D7 R1	1	0.02	2.08	100.00		2.06	97.54	0.12	0.38	0.18	0.08
24	03 SS207 5C 6m D7 R3	1		2.21	100.00		2.21	97.41	0.12	0.38	0.17	0.09
25	03 SS207 5C 9m D3 S1	1	0.03	1.42	100.00	0.01	1.38	98.58				
26	03 SS207 5C 9m D3 S2	1		0.99	100.00		0.99	99.01				
27	03 SS207 5C 9m D3 S3	1	0.02	1.20	100.00		1.17	98.80				
28	03 SS207 5C 9m D3 S4	1	0.02	1.05	100.00		1.03	98.93	0.02	0.02		
29	03 SS207 5C 9m D7 R1	1		0.96	100.00		0.96	99.02		0.02	0.02	
30	03 SS207 5C 9m D7 R3	1	0.03	0.94	100.00		0.91	99.06				
31	VGTO -S258 Syr 2 25C B	1		2.57	100.00		2.57	97.43				
32	03 EF-7630-13 10mg/mL 20ug	1	0.01	2.19	100.00		2.14	97.81				
33	WFI	1			100.00			100.00				
34	03 SS207 5C 12m D3 S1	1		1.25	100.00	0.01	1.24	98.74		0.01	0.01	
35	03 SS207 5C 12m D3 S2	1		0.99	100.00		0.99	99.01				
36	03 SS207 5C 12m D3 S3	1		0.97	100.00		0.97	99.01	0.02	0.02		
37	03 SS207 5C 12m D3 S4	1	0.01	0.98	100.00		0.98	98.98	0.01	0.04	0.02	
38	03 SS207 5C 12m D7 R1	1	0.02	0.93	100.00		0.93	99.03	0.01	0.04	0.02	

080220 Max process Part 3

Component Summary Export2

Component Summary For Area

#	Sample Name	Inj	Agg 2	Agg 1	Total Agg	Total VEGFT	Native	Total Deg	Deg 1	Deg 2	Deg 3	
1	03 SS207 5C 15m D3 S2	1		795618	795618	73103317	72276398	31301	9279	9308	12714	
2	03 SS207 5C 15m D3 S3	1		803424	803424	74001128	73161642	36062		17528	18534	
3	03 SS207 5C 15m D3 S4	1		760673	760673	72045912	71254218	31021		17753	13268	
4	03 SS207 5C 15m D7 R1	1	7746	1345177	1374125	87751879	86346230	31524	5745	11205	14574	
5	03 SS207 5C 15m D7 R2	1		857080	857080	76733831	75862104	14646			14646	
6	03 SS207 5C 18m D3 S1	1		828662	828662	71845054	70978058	38334		23472	14862	
7	03 EF-7630-13 10mg/mL 20ug	1		1621130	1637411	74634588	72997177		6768			
8	03 SS207 5C 18m D3 S2	1		807424	807424	72438673	71594979	36270	13766	8721	13784	
9	03 SS207 5C 15m D3 S1	1		807060	807060	71024831	70184918	32853	10150	9793	12909	
10	03 SS207 5C 18m D3 S3	1		829432	829432	73383968	72517606	36930	12524	11190	13217	
11	03 SS207 5C 18m D3 S4	1		819822	819822	74352191	73475964	56406	9410	12096	17657	17243
12	03 SS207 5C 18m D7 R1	1		975925	975925	75588299	74561510	50864		27860	23004	
13	03 SS207 5C 24m D3 S1	1		1014211	1014211	76611963	75528958	68795	15037	11968	27756	14034
14	03 SS207 5C 24m D3 S4	1		953678	953678	73712330	72712913	45739		29498	16241	
15	03 SS207 5C 24m D7 R1	1		934919	934919	72970294	71990186	45190		24925	20265	
16	03 SS207 5C 4m D7 R1	1	10340	474756	2675563	78290801	75615238		2190466			
17	03 SS207 5C 4m D7 R3	1		612384	612384	73792586	73180202					
18	03 EF-7630-13 10mg/mL 20ug	1		1640508	1653707	75270160	73616453		13199			

Component Summary For Amount

#	Sample Name	Inj	Total VEGFT	Total Agg	Total Deg
1	03 SS207 5C 15m D3 S2	1	19.336		
2	03 SS207 5C 15m D3 S3	1	19.58		
3	03 SS207 5C 15m D3 S4	1	19.048		
4	03 SS207 5C 15m D7 R1	1	23.318		
5	03 SS207 5C 15m D7 R2	1	20.323		
6	03 SS207 5C 18m D3 S1	1	18.994		
7	03 EF-7630-13 10mg/mL 20ug	1	19.752		
8	03 SS207 5C 18m D3 S2	1	19.155		
9	03 SS207 5C 15m D3 S1	1	18.771		
10	03 SS207 5C 18m D3 S3	1	19.412		
11	03 SS207 5C 18m D3 S4	1	19.675		
12	03 SS207 5C 18m D7 R1	1	20.011		
13	03 SS207 5C 24m D3 S1	1	20.29		
14	03 SS207 5C 24m D3 S4	1	19.501		
15	03 SS207 5C 24m D7 R1	1	19.3		
16	03 SS207 5C 4m D7 R1	1	20.746		
17	03 SS207 5C 4m D7 R3	1	19.523		
18	03 EF-7630-13 10mg/mL 20ug	1	19.925		

Component Summary For Concentration

#	Sample Name	Inj	Calibration Id	Result Id	Cal Curve Id	Total VEGFT	Total Agg	Total Deg
1	03 SS207 5C 15m D3 S2	1	9388	9831	9390	38.672		
2	03 SS207 5C 15m D3 S3	1	9388	9832	9390	39.16		
3	03 SS207 5C 15m D3 S4	1	9388	9833	9395	38.097		
4	03 SS207 5C 15m D7 R1	1	9388	9834	9391	46.635		
5	03 SS207 5C 15m D7 R2	1	9388	9835	9390	40.645		
6	03 SS207 5C 18m D3 S1	1	9388	9836	9390	37.988		
7	03 EF-7630-13 10mg/mL 20ug	1	9388	9844	9391	9.876		
8	03 SS207 5C 18m D3 S2	1	9388	9837	9391	38.31		
9	03 SS207 5C 15m D3 S1	1	9388	9830	9390	37.542		
10	03 SS207 5C 18m D3 S3	1	9388	9838	9390	38.824		
11	03 SS207 5C 18m D3 S4	1	9388	9839	9390	39.351		
12	03 SS207 5C 18m D7 R1	1	9388	9840	9390	40.023		
13	03 SS207 5C 24m D3 S1	1	9388	9841	9390	40.579		
14	03 SS207 5C 24m D3 S4	1	9388	9842	9390	39.003		
15	03 SS207 5C 24m D7 R1	1	9388	9843	9390	38.599		
16	03 SS207 5C 4m D7 R1	1	9388	9846	9391	41.492		
17	03 SS207 5C 4m D7 R3	1	9388	9847	9391	39.046		
18	03 EF-7630-13 10mg/mL 20ug	1	9388	9845	9390	9.962		

Component Summary For % Area

#	Sample Name	Inj	Agg 2	Agg 1	Total Agg	Total VEGFT	Native	Total Deg	Deg 1	Deg 2	Deg 3	
1	03 SS207 5C 15m D3 S2	1		1.09	1.09	100	98.87	0.04	0.01	0.01	0.02	
2	03 SS207 5C 15m D3 S3	1		1.09	1.09	100	98.87	0.05		0.02	0.03	
3	03 SS207 5C 15m D3 S4	1		1.06	1.06	100	98.9	0.04		0.02	0.02	
4	03 SS207 5C 15m D7 R1	1	0.01	1.53	1.57	100	98.4	0.04	0.01	0.01	0.02	
5	03 SS207 5C 15m D7 R2	1		1.12	1.12	100	98.86	0.02			0.02	
6	03 SS207 5C 18m D3 S1	1		1.15	1.15	100	98.79	0.05		0.03	0.02	
7	03 EF-7630-13 10mg/mL 20ug	1		2.17	2.19	100	97.81		0.01			
8	03 SS207 5C 18m D3 S2	1		1.11	1.11	100	98.84	0.05	0.02	0.01	0.02	
9	03 SS207 5C 15m D3 S1	1		1.14	1.14	100	98.82	0.05	0.01	0.01	0.02	
10	03 SS207 5C 18m D3 S3	1		1.13	1.13	100	98.82	0.05	0.02	0.02	0.02	
11	03 SS207 5C 18m D3 S4	1		1.1	1.1	100	98.82	0.08	0.01	0.02	0.02	0.02
12	03 SS207 5C 18m D7 R1	1		1.29	1.29	100	98.64	0.07		0.04	0.03	
13	03 SS207 5C 24m D3 S1	1		1.32	1.32	100	98.59	0.09	0.02	0.02	0.04	0.02
14	03 SS207 5C 24m D3 S4	1		1.29	1.29	100	98.64	0.06		0.04	0.02	
15	03 SS207 5C 24m D7 R1	1		1.28	1.28	100	98.66	0.06		0.03	0.03	
16	03 SS207 5C 4m D7 R1	1	0.01	0.61	3.42	100	96.58		2.8			
17	03 SS207 5C 4m D7 R3	1		0.83	0.83	100	99.17					
18	03 EF-7630-13 10mg/mL 20ug	1		2.18	2.2	100	97.8		0.02			

Graham Ex. 5

NOTEBOOK NO. 6223

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ON February 13, 2004

DEPARTMENT

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2) Entries should be made in permanent ink - do not use pencil.

3) The title should be accurately recorded when starting a page.

4) All data is to be recorded directly into the notebook. The inclusion of all elaborate details is preferable. Notes and calculations should not be done on loose paper. In the case of error, draw a single line through the incorrect data. Do not erase or use correction fluid. All corrections should be initialed and dated.

5) After entering your data, sign and date all entries. Witness or witnesses should sign and date each entry in the spaces provided. The witnesses must observe the work that is done and have sufficient knowledge to understand what they have read. Names of operators and witnesses present during any demonstration should be recorded.

6) This notebook, and all information recorded therein, are the exclusive property of the Company. All contents of this book are **strictly confidential.** It must be returned when completed, upon request, or upon termination of employment. It should be kept in a protected place to safeguard against loss. If the book is lost, the supervisor should be notified immediately, and a written report describing the circumstances should be submitted.

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RGN-EYLEA-BIOSIM-00477345

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Name: Kelly Frye

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Project No. VEGF Trap

TITLE VGFT-SS195

Book No. 6223

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OBJECTIVE: See protocol below

Protocol For Stability
Study #VGFT-195

Purpose:

There are plans to administer VEGF Trap to the eye. The required concentration to achieve the doses planned in the clinical study is thought to be either 10 mg/mL or 40 mg/mL VEGF Trap. An iso-osmolar solution is highly desired for ocular delivery. A formulation containing 135mM NaCl will yield an iso-osmolar solution.

Data from stability studies VGFT-SS183, SS186, SS187, SS189, SS192, SS193, and SS194 indicate that there is a problem with the physical stability of VEGF Trap in the current ITV formulation above 10 mg/mL VEGF Trap. Specifically, particulate is seen after the high concentration formulations are pulled up into a syringe and ejected into a vial. Therefore, a more stable ITV formulation is essential. Stability studies VGFT-SS126 and VGFT-SS138 investigated the stability of VEGF Trap in the presence of sucrose. The results indicate that the stability of VEGF Trap is directly proportional to the concentration of sucrose in the formulation. Those stability studies examined formulations with up to 5% sucrose. An iso-osmolar formulation can be achieved with 7% sucrose if the NaCl is completely removed.

In addition, the clinical ITV formulation has been shown to be prone to precipitate when vortexed (VGFT-SS146, SS149, and SS155). VEGF Trap no longer precipitated upon vortex when the clinical DP was spiked with 0.03% Polysorbate 20.

This stability study is designed to determine what are the lead formulations that should be filled into prefilled syringes in an upcoming development fill at Vetter. The stability of VEGF Trap in formulations containing either polysorbate 20 or a combination of polysorbate 20 and PEG 3350 with either 5% or 7% sucrose will be examined.

Procedure:

The basic formulation for each formulation is

10 mM Phosphate
0.03% Polysorbate 20
40 mg/mL VEGF Trap
pH 6.25

KJF 11-23-05

Each formulation will have the following modifications:

Formulation #	Lot #	[NaCl] (mM)	[Sucrose] (%)	PEG 3350	Density (g/mL)
1	L05-255	40	5	0.1	1.031
2	L05-256	40	5	-	1.031
3	L05-257	0	7	0.1	1.038
4	L05-258	0	7	-	1.038
5	L05-259	135	-	0.1	1.011

Where PS 20 is polysorbate 20.

Preparation:

The Formulation Development Group at Regeneron Pharmaceuticals, Inc., Tarrytown, NY will prepare 3.4 mL of each formulation. The formulation will be filter sterilized, using a syringe and Millex-GV 0.2 µM filter with a Durapore membrane (PVDF). Filter sterilization and filling of vials will be performed in a laminar flow hood.

Each formulation will be dispensed in the laminar flow hood as follows: Three (3) 3 mL glass vial will be filled with 0.25 mL of formulation (agitation study). Eleven (11) 3 mL glass vials will be filled with 0.2 mL of formulated VEGF Trap (thermal studies, freeze/thaw studies, and t=0).

Storage Conditions:

Each formulation will be subjected to the following set of stress tests.

Agitation Study: Three (3) glass vials containing 0.25 mL of each formulation will be used in the agitation study. The vials will be vortexed at room temperature at speed = 4. One vial will be removed after 30, 60 and 120 minutes (a visual inspection will be done at 90 minutes).

Thermal Studies (45°C): Three (3) 3-mL glass vials, containing 0.2 mL per vial of each formulation, will be placed in the 45°C chamber. One vial will be removed after 3, 7, and 14 days of incubation.

Thermal Studies (37°C): Three (3) 3-mL glass vials, containing 0.2 mL per vial of each formulation, will be placed in the 37°C chamber. One vial will be removed after 3, 7, and 14 days of incubation.

Thermal Studies (25°C): Two (2) 3-mL glass vials, containing 0.2 mL per vial of each formulation, will be placed in the 25°C chamber. One vial will be removed after 14 and 28 days of incubation.

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Project No. VEGF Trap

TITLE VGFT-SS195

Book No. 6223

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T=0 Sample (-80°C): One (1) 3-mL glass vial, containing 0.2 mL per vial, will be placed in the -80°C chamber. This vial will be designated as t=0.

Freeze/Thaw Studies: Two (2) 3 mL glass vials, containing 0.2 mL of each formulation, will be used to examine the stability of the protein when frozen and thawed. The vials will be frozen by placing them in an -80°C freezer, for a minimum of 45 min, and thawed by placing them on a bench top at room temperature for 30 minutes. After each freeze/thaw cycle, the vials will be mixed by gently inverting them 5 times. The vial will be frozen and thawed 4 and 8 times respectively.

Analyses To Be Performed:

Osmolality: The osmolality of the formulations will be measured and recorded after they are manufactured.

Visual Inspection: Each vial will be gently inverted and then visually inspected for the presence of particulates. The appearance of particulates in the solution will be recorded. If no precipitation is found, the result "clear, no ppt" will be recorded. Any other problem that is found will be recorded. Such problems may involve the integrity of the vial and the container closure system.

Physical Stability: Optical density (OD 405 nm) will be performed on every sample in this stability study. These measurements will be made using 150 µL of sample and the microplate reader. Optical density, at 405 nm, measures the turbidity and therefore can be indicative of the presence of precipitation. The pH of all thermally stressed samples will be measured. After both pH and OD measurements, the sample will be returned to the vial and used for further analysis.

SEC-HPLC analysis will be performed to determine the amount of protein that is actually recovered in all samples.

Chemical stability: SEC-HPLC will be performed on all samples to determine the chemical stability of VEGF Trap. Any other assay that is either developed or is deemed of interest may be performed. This may include RP-HPLC, SDS-PAGE, IEF or DSC.

KJF 11-23-05

Data Analysis:

All data will be kept in research notebooks. Original copies of gels, chromatograms, protocols, pull schedules etc. will be kept in the study file. When all analyses are complete the samples generated in the experiment may be destroyed.

Approvals:

The study director must approve this protocol.

Study Coordinator — Date 10/10/05

Study Director — Date 10-11-05

KJF 11-23-05

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TITLE VGFT-SS195 Project No. VEGF Trap Book No. 6223

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Calculations:

Prepare 4.4 mL of each formulation

D.S → 100.43 mg/mL VEGF Trap in 10mM phosphate, pH 6.25 density = 1.0283 g/mL

Protein (4.4mL)(40mg/mL) = (X)(100.43mg/mL)

X = 1.752mL OR 1.802g

Phosphate KF 9-30-05

want ~~need~~ (4.4m)(10mM) = 44 μmoles

have (1.752mL)(10mM) = 17.52 μmoles

need 44 − 17.52 μmoles = 26.48 μmoles

from 100mM Phos. stock soln 0.2648 mL of 100mM Phos

Polysorbate 20 from 1% stock

(4.4mL)(0.03%) = (X)(1%)

X = 0.132mL of 1% stock

NaCl from 300mM stock

F1 & F2 (4.4mL)(40mM) = (X)(300mM)

X = 0.5867mL of stock

F5 (4.4mL)(135mM) = (X)(300mM)

X = 1.98mL of stock

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Sucrose

F1 & F2 $\frac{5g}{100mL} \times 4.4mL = 0.22g$

F3 & F4 $\frac{7g}{100mL} \times 4.4mL = 0.308g$

PEG 3350 from 5% stock

F1, F3, & F5 (4.4mL)(1%) = (X)(5%)

X = 0.088mL of stock

F1 : lot # L05-255 density = 1.031 g/mL

Lot #/Manufacturer	Reagent	Theoretical	Actual
	WFI	1.4429g	1.44g
JD-7147-02 / Regn	100mM Phosphate	0.2648g	0.27g
~~JD-7147-05 / Regn~~	300mM NaCl	0.5867g	0.59g
B07H10 / Mallinckrodt	Sucrose	0.22g	0.2207g
JD-7147-01 / Regn	5% PEG 3350	0.088g	88μl
JD-7147-04 / Regn	1% Polysorbate 20	0.132g	132μl
FD050615P / Regn	100.43mg/mL VEGF Trap	1.802g (1.752mL)	1.81g ~~1.80g~~ 1.75g

final wgt. 4.5364g

pH 6.25 initial 6.14

+1μl of 1N NaOH to adjust pH before protein final 6.24

initial + protein 6.35

+2μl 1N HCl final + protein 6.27

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Project No. VEGF Trap

TITLE VGFT-SS195 Book No. 6223

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F2: lot # L05-256 density = 1.031 g/mL

Mfr. / Lot#	Reagent	Theoretical	Actual
	WFI	1.5309g	1.53g
JD-7147-02/Regn	100mM Phosphate	0.2648g	0.27g
JD-7147-05/Regn	300mM NaCl	0.5867g	0.59g
B07H10/Mallinckrodt	Sucrose	0.22g	0.2202g
JD-7147-04/Regn	1% polysorbate 20	0.132g	132µl
FD050615P/Regn	100.43mg/mL VEGF Trap	1.802g (1.752mL)	1.80g
	final wgt.	4.5364g	

pH 6.25 initial 6.17
+ 0.8µl of 1N NaOH Before protein final 6.25
6.34 pH after protein +2µl 1N HCl after protein 6.28

F3: lot # L05-257 density = 1.038 g/mL

lot# / Mfr.	Reagent	Theoretical	Actual
	WFI	1.9724g	1.97g
JD-7147-02/Regn	100mM phosphate	0.2648g	0.26g
B07H10/Mallinckrodt	sucrose	0.308g	0.3084g
JD-7147-01/Regn	5% PEG3350	0.088g	88µl
JD-7147-04/Regn	1% polysorbate 20	0.132g	132µl
FD050615P/Regn	100.43mg/mL VEGF Trap	1.802g (1.752mL)	1.80g
	final wgt.	4.5672g	

pH 6.25 initial 6.35
+1µl 1N HCl before protein 6.24
final 6.28

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Project No. VEGF Trap

TITLE VGFT-SS195 Book No. 6223

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F4: Lot L05-258 density = 1.038 g/mL

lot#/Mfr.	Reagent	Theoretical	Actual
	WFI	2.0604g	2.06g
JD-7147-02/Regn	100mM Phosphate	0.2648g	0.26g
B07H10/Malinckrod	sucrose	0.308g	0.3081g
JD-7147-04/Regn	1% polysorbate 20	0.132g	132µl
FD050615P/Regn	100.43mg/mL VEGF Trap	1.802g (1.752mL)	1.80g
	final wgt.	4.5672g	

pH 6.25 initial 6.31
+ 0.8µl 1N HCl + 0.5µl 0.5N NaOH before protein 6.25
final 6.24

F5: Lot# L05-259 density = ~~1.03~~ 1.011 g/mL KSF 9-30-05

Mfr / lot#	Reagent	Theoretical	Actual
	WFI	0.1816g	0.18g
JD-7147-02/Regn	100mM Phosphate	0.2648g	0.26g
JD-7147-02/Regn	300mM NaCl	1.98g	1.99g
JD-7147-01/Regn	5% PEG3350	0.088g	88µl
JD-7147-04/Regn	1% polysorbate 20	0.132g	132µl
FD050615P/Regn	100.43mg/mL VEGF Trap	1.802g (1.752mL)	1.80g
	final wgt.	4.4484g	

pH 6.25 initial 6.07
+1.6µl 1N NaOH + 0.5µl 0.5N NaOH before protein 6.24
final 6.28
6.29 pH after protein +0.5µl 0.5N HCl

Calculations checked by: Kathe Bowen 9/30/05

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Regeneron Ex. 2024
Formycon v. Regeneron
IPR2025-00233
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Graham Ex. 6

					SS 195; 45C							
Formulation	Length of Stress	HMW Peak Area	HMW Peak Area	HMW Peak Area	Native Peak Area	LMW Peak Area	LMW Peak Area	VEGF-TRAP mg/ml	% VEGF-TRAP Recov-ered	% Native VEGF-TRAP	% HMW Species	% LMW Species
	Time			(33')	(38')							
#1	T=0	0	0	1756	75560	0	0	40.71	100	97.7	2.3	0.0
	3d	89	682	5930	70112	133	307	40.68	100	90.8	8.7	0.6
	7d	491	1795	10503	64764	121	279	41.05	101	83.1	16.4	0.5
	T=0	19	59	2091	79306	0	0	39.17	100	97.3	2.7	0.0
	14D	1345	4292	14546	58463	435	474	38.23	98	73.5	25.4	1.1
#2	T=0	0	54	1689	72996	0	0	39.34	100	97.7	2.3	0.0
	3d	101	637	6079	71950	122	259	41.69	106	90.9	8.6	0.5
	7d	428	1788	9964	63445	126	331.82	40.06	102	83.4	16.0	0.6
	T=0	23	45	1970	78007	124	0	38.53	100	97.3	2.5	0.2
	14d	1259	4280	14809	59168	423	454	38.64	100	73.6	25.3	1.1
#3	T=0	0	0	1813	76053	0	0	41.01	100	97.7	2.3	0.0
	3d	73	523	4903	71091	115	193	40.49	99	92.4	7.2	0.4
	7d	340	1209	8383	65794	133	266.00	40.08	98	86.4	13.0	0.5
	T=0	21	50	2028	77235	133	0	38.19	100	97.2	2.6	0.2
	14d	845	3004	13128	64240	379	336.00	39.39	103	78.4	20.7	0.9
#4	T=0	0	0	1805	73352	0	0	39.56	100	97.6	2.4	0.0
	3d	69	434	4876	70620	91	208	40.17	102	92.6	7.0	0.4
	7d	256	1314	7900	65358	122	283	39.60	100	86.9	12.6	0.5
	t=0	43	60	2210	78406	140	0	38.87	100	97.0	2.9	0.2
	14d	698	2890	12237	63092	414	432	38.33	99	79.1	19.8	1.1
#5	T=0	0	0	1770	74801	0	0	40.32	100	97.7	2.3	0.0
	3d	430	1012	9066	62962	113	233	38.85	96	85.3	14.2	0.5
	7d	2073	3574	14660	53609	125	297	39.13	97	72.1	27.3	0.6
	T=0	39	84	2059	79894	0	0	39.46	100	97.3	2.7	0.0
	14d	5191	8016	18591	46176	344	396	37.83	96	58.7	40.4	0.9

Sequence Number : 093005G												
Std Curve used: 40mg/mL (093005G)												
14 d sequence # 101205H												

SS 195; 25C

Formulation	Length of Stress Time	HMW Peak Area	HMW Peak Area	HMW Peak Area (33')	Native Peak Area (38')	LMW Peak Area	LMW Peak Area	VEGF-TRAP mg/ml	% VEGF-TRAP Recov-ered
#1	T=0	19	59	2091	79306	0	0	39.17	100
	14d	0	69	2428	77224	186	0	38.40	98
	t=0	0	41	1034	79800	0	0	39.37	100
	28d	0	92	2640	78103	252	0	39.48	100
#2	**T=0**	23	45	1970	78007	124	0	38.53	100
	14d	0	74	2379	77023	167	0	38.28	99
	t=0	0	38	1931	79718	0	0	39.78	100
	28d	0	146	2674	78228	312	0	39.61	100
#3	**T=0**	21	50	2028	77235	133	0	38.19	100
	14d	0	73	2465	76462	187	0	38.06	100
	t=0	0	44	2041	79525	0	0	39.74	100
	28d	0	105	2698	77219	277	0	39.08	98
#4	**t=0**	43	60	2210	78406	140	0	38.87	100
	14d	25	66	2514	78695	211	0	39.18	101
	t=0	0	57	2199	80388	0	0	40.26	100
	28d	0	95	2668	77631	279	0	39.27	98
#5	T=0	39	84	2059	79894	0	0	39.46	100
	14d	0	89	2436	76132	171	0	37.88	96
	t=0	0	52	2021	81572	0	0	40.76	100
	28d	0	117	2663	77082	322	0	39.02	96

14 d sequence # 101205H
28d sequence # 102605H

% Native VEGF-TRAP	% HMW Species	% LMW Species
97.3	2.7	0.0
96.6	3.1	0.2
98.7	1.3	0.0
96.3	3.4	0.3
97.3	2.5	0.2
96.7	3.1	0.2
97.6	2.4	0.0
96.2	3.5	0.4
97.2	2.6	0.2
96.6	3.2	0.2
97.4	2.6	0.0
96.2	3.5	0.3

97.0	2.9	0.2
96.5	3.2	0.3
97.3	2.7	0.0
96.2	3.4	0.3

97.3	2.7	0.0
96.6	3.2	0.2
97.5	2.5	0.0
96.1	3.5	0.4

SS 195; 37C

Formulation	Length of Stress	HMW Peak Area	HMW Peak Area	HMW Peak Area	Native Peak Area	LMW Peak Area	LMW Peak Area	VEGF-TRAP mg/ml	% VEGF-TRAP Recov-ered	% Native VEGF-TRAP	% HMW Species	% LMW Species
	Time			(33')	(38')							
#1	T=0	0	0	1756	75560	0	0	40.71	100	97.7	2.3	0.0
	3d	19	120	2831	73019	70	165	40.13	99	95.8	3.9	0.3
	7d	32	398	4280	72774	86	244	40.98	101	93.5	6.1	0.4
	T=0	19	59	2091	79306	0	0	39.17	100	97.3	2.7	0.0
	14D	25	669	5913	72392	403	0	38.16	97	91.2	8.3	0.5
#2	T=0	0	54	1689	72996	0	0	39.34	100	97.7	2.3	0.0
	3d	22	136	2875	72193	87	173	39.74	101	95.6	4.0	0.3
	7d	23	377	4160	71224	75	248	40.07	102	93.6	6.0	0.4
	T=0	23	45	1970	78007	124	0	38.53	100	97.3	2.5	0.2
	14d	20	704	5762	72207	410	426	38.22	99	90.8	8.2	1.1
#3	T=0	0	0	1813	76053	0	0	41.01	100	97.7	2.3	0.0
	3d	19	148	2817	72983	89	147	40.12	98	95.8	3.9	0.3
	7d	30	302	3759	71765	64	196	40.07	98	94.3	5.4	0.3
	T=0	21	50	2028	77235	133	0	38.19	100	97.2	2.6	0.2
	14d	30	511	5307	73264	450	406	38.43	101	91.6	7.3	1.1
#4	T=0	0	0	1805	73352	0	0	39.56	100	97.6	2.4	0.0
	3d	41	168	2792	72862	73	130	40.05	101	95.8	3.9	0.3
	7d	46	337	3634	70680	77	128	39.43	100	94.4	5.4	0.3
	t=0	43	60	2210	78406	140	0	38.87	100	97.0	2.9	0.2
	14d	20	483	5064	73081	360	0	37.97	98	92.5	7.0	0.5
#5	T=0	0	0	1770	74801	0	0	40.32	100	97.7	2.3	0.0
	3d	0	428	3566	72266	92	177	40.29	100	94.4	5.2	0.4
	7d	36	784	5390	68228	127	92	39.30	97	91.4	8.3	0.3
	T=0	39	84	2059	79894	0	0	39.46	100	97.3	2.7	0.0
	14d	1398	8091	68340	386	367	0	37.76	96	0.5	99.0	0.5

Sequence Number : 093005G
Std Curve used: 40mg/mL (093005G)

14 d sequence # 101205H

SS 195 Freeze Thaw

Formulation	Length of Stress	HMW Peak Area	HMW Peak Area	HMW Peak Area	Native Peak Area	LMW Peak Area	LMW Peak Area	VEGF-TRAP mg/ml	% VEGF-TRAP Recov-ered	% Native VEGF-TRAP	% HMW Species	% LMW Species
	Time			(33')	(38')							
#1	T=0	0	0	1756	75560	0	0	40.71	100	97.7	2.3	0.0
	4x FT	0	0	1849	73930	0	0	39.90	98	97.6	2.4	0.0
	8x FT	0	0	1801	73305	0	0	39.54	97	97.6	2.4	0.0
#2	T=0	0	54	1689	72996	0	0	39.34	100	97.7	2.3	0.0
	4x FT	0	0	1792	72451	0	0	39.08	99	97.6	2.4	0.0
	8x FT	0	0	1804	73274	0	0	39.52	100	97.6	2.4	0.0
#3	T=0	0	0	1813	76053	0	0	41.01	100	97.7	2.3	0.0
	4x FT	0	0	1780	72337	0	0	39.01	95	97.6	2.4	0.0
	8x FT	0	0	1812	73444	0	0	39.62	97	97.6	2.4	0.0
#4	T=0	0	0	1805	73352	0	0	39.56	100	97.6	2.4	0.0
	4x FT	0	0	1762	72859	0	0	39.28	99	97.6	2.4	0.0
	8x FT	0	0	1827	73957	0	0	39.90	101	97.6	2.4	0.0
#5	T=0	0	0	1770	74801	0	0	40.32	100	97.7	2.3	0.0
	4x FT	0	53	1667	72754	0	0	39.20	97	97.7	2.3	0.0
	8x FT	0	0	1848	74254	0	0	40.07	99	97.6	2.4	0.0

Sequence no: 093005G
Std Curve used: 40mg/mL (093005G)

Stability Study VGT-SS195

Formulation	Length of Stress (hours)	HMW Peak Area	HMW Peak Area	HMW Peak Area (33')	Native Peak Area (38')	LMW Peak Area	LMW Peak Area	[VEGF-TRAP] mg/ml	% VEGF-TRAP Recov-ered	% Native VEGF-TRAP	% HMW Species	% LMW Species
#1	T=0	0	0	1756	75560	0	0	40.71	100	97.7	2.3	0.0
10 mM Phosphate,	30m VA	0	0	1731	74452	0	0	40.11	99	97.7	2.3	0.0
40 mM NaCl,	30m VB	0	0	1732	73523	0	0	39.62	97	97.7	2.3	0.0
0.03% PS20	60m VA	0	0	1756	76059	0	0	40.98	101	97.7	2.3	0.0
0.1%PEG 3350	60m VB	0	66	1727	75373	0	0	40.63	100	97.7	2.3	0.0
5% Sucrose	120m VA	0	0	1781	73940	0	0	39.86	98	97.6	2.4	0.0
40 mg/mL VEGFT	120m VB	0	83	1825	77466	0	0	41.81	103	97.6	2.4	0.0
pH 6.25												
#2	T=0	0	54	1689	72996	0	0	39.34	100	97.7	2.3	0.0
10 mM Phosphate,	30m VA	0	46	1725	74821	0	0	40.33	103	97.7	2.3	0.0
40 mM NaCl,	30m VB	0	0	1840	76399	0	0	41.21	105	97.6	2.4	0.0
0.03% PS20	60m VA	0	61	1712	74505	0	0	40.16	102	97.7	2.3	0.0
5% Sucrose	60m VB	0	0	1804	75936	0	0	40.94	104	97.7	2.3	0.0
40 mg/mL VEGFT	120m VA	0	0	1781	75280	0	0	40.58	103	97.7	2.3	0.0
pH 6.2	120m VB	0	0	1765	75521	0	0	40.70	103	97.7	2.3	0.0
#3	T=0	0	0	1813	76053	0	0	41.01	100	97.7	2.3	0.0
10 mM Phosphate,	30m VA	18	53	1720	72907	0	0	39.32	96	97.6	2.4	0.0
0.03% PS20	30m VB	0	0	1758	73584	0	0	39.66	97	97.7	2.3	0.0
0.1%PEG 3350	60m VA	0	0	1831	75925	0	0	40.95	100	97.6	2.4	0.0
7% Sucrose	60m VB	0	0	1808	76310	19	0	41.15	100	97.7	2.3	0.0
40 mg/mL VEGFT	120m VA	0	0	1780	74939	0	0	40.40	99	97.7	2.3	0.0
pH 6.25	120m VB	0	0	1826	74779	0	0	40.34	98	97.6	2.4	0.0
#4	T=0	0	0	1805	73352	0	0	39.56	100	97.6	2.4	0.0
10 mM Phosphate,	30m VA	0	0	1787	73553	0	0	39.66	100	97.6	2.4	0.0
0.03% PS20	30m VB	0	0	1794	74744	0	0	40.30	102	97.7	2.3	0.0
7% Sucrose	60m VA	0	0	1732	73135	0	0	39.41	100	97.7	2.3	0.0
40 mg/mL VEGFT	60m VB							-0.48				
pH 6.25	120m VA	0	0	1748	73157	0	0	39.43	100	97.7	2.3	0.0
	120m VB	0	76	1763	74734	0	0	40.32	102	97.6	2.4	0.0
#5	T=0	0	0	1770	74801	0	0	40.32	100	97.7	2.3	0.0
10 mM Phosphate,	30m VA	0	69	1696	72773	0	0	39.23	97	97.6	2.4	0.0
135 mM NaCl,	30m VB	0	51	1730	74524	0	0	40.18	100	97.7	2.3	0.0
0.03% PS20	60m VA	0	56	1796	74369	0	0	40.13	100	97.6	2.4	0.0
0.1%PEG 3350	60m VB	0	0	1748	72472	0	0	39.06	97	97.6	2.4	0.0
40 mg/mL VEGFT	120m VA	0	70	1729	74752	0	0	40.31	100	97.6	2.4	0.0
pH 6.25	120m VB	0	0	1765	74198	0	0	39.99	99	97.7	2.3	0.0
Sequence Number : 093005G												
Std Curve used: 40mg/mL (093005G)												