

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
103928Orig1s000

OTHER REVIEW(S)

MEMORANDUM

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research

DATE: July 1, 2004

FROM: Dale Slavin, Ph.D.
Regulatory Project Manager
Division of Application Review Management and Policy, HFM-588
Office of Drug Evaluation VI

TO: STN 103928/0

SUBJECT: SBA Equivalent for

- Product: Technetium (99m Tc) Fanolesomab [NeutroSpec™]
- Manufacturer: Palatin Technologies
- License Number: 1588

Indications and Usage

Technetium (99m Tc) Fanolesomab is indicated for scintigraphic imaging of patients with equivocal signs and symptoms of appendicitis who are five years of age or older.

Dosage Form, Route of Administration, and Recommended Dosage

Extract relevant information from approved draft labeling and include whether:

Kit containing the following:

One 3 mL single use vial of fanolesomab as a sterile, non-pyrogenic, lyophilized mixture of 0.25 mg fanolesomab; 12.5 mg maltose monohydrate; 0.522 mg sodium potassium tartrate tetrahydrate, USP; 0.221 mg succinic acid; 54 µg stannous tartrate (minimum stannous 7 µg; maximum total stannous and stannic tin 24 µg); 28 µg glycine, USP; and 9.3 µg disodium edetate dihydrate, USP. The lyophilized powder contains no preservatives and has no US standard of potency.

One 2 mL ampule Cenolate™ [Ascorbic Acid Injection, USP (500 mg/mL)] - Diluent

Fanolesomab when reconstituted with Technetium Tc 99m and Cenolate is designed to deliver a 75-125 mcg dose labeled with 10-20 mCi Technetium Tc 99m and must be administered IV.

Basis for Approval

The following reviews, filed in the CBER correspondence section of the license file for STN 103928/0, comprise the SBA equivalent for this application/supplement:

<u>Discipline</u>	<u>Reviewer Name</u>	<u>Date</u>
CMC		
Product	Leon Epps, PharmD	6-5-00
Product	Chana Fuchs, PhD	9-13-00
Product	Fuchs, PhD/Epps, PharmD/Frucht, MD	6-21-04
Facility	D. Trout	3-31-04
Facility	M. Swider	7-1-04
<u>Clinical/PreClin/Stat</u>		
Clinical	R. Lindblad, MD	9-1-00
Clinical	K. Ayalew, MD/I. Marzella, MD	6-15-04
Clin/Nuc Med	L. Martynec	3-20-04
PreClin/Clin Pharm	M. Green, PhD	7-1-04
Statistical	S. Misra, PhD	7-1-04
BiMo	M. Andrich, MD	1-31-01
BiMo	L. Johnson, PharmD	3-15-04
Labeling	F. Duffy, RN	3-26-04
Tertiary Review	M. Walton, MD, PhD	6-30-04



DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research

Memorandum

Date: June 28, 2004
From: Dale Slavin, Ph.D. OTRR/DARP
Subject: NeutroSpec - PI
To: BLA STN 103928/0 Palatin Technologies

I spoke to Dr. Kaushik Dave and told him that I would e-mail him other minor changes to the package insert. I subsequently e-mailed him both clean and redlined copies of the PI. In the e-mail I explained that none of the references were considered to add any information to the PI so these had been removed. I also stated that the wording (b) (4)

(b) (4) I have included the redlined PI.

14 Pages of Draft Labeling have been Withheld in Full as b4 (CCI/TS)
immediately following this page

FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF NEW DRUGS
OFFICE OF DRUG EVALUATION VI
DIVISION OF REVIEW MANAGEMENT AND POLICY

Woodmont Office Complex II, 6th Floor
1451 Rockville Pike
Rockville, Maryland 20852-1448
FAX #: 301-827-5397

FACSIMILE TRANSMISSION RECORD

TOTAL NUMBER OF PAGES: 4 (Including Cover Page)
FAX TO: Kaushik Dave
Facsimile Telephone No. 1-609-495-2201 Voice Telephone No. 1-609-495-2200
FROM: Kay Schneider
Facsimile Telephone No. 301-827-5397 Voice Telephone No. 301-827-4358
DATE: 6-25-04 TIME: 5:45 pm
MESSAGE: Attached are the PMCs (DRAFT)
for your consideration.

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW. If you are not the addressee, or a person authorized to deliver the document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us at the above address by mail. Thank you.

Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

1. Please provide a commitment to evaluate the clinical performance and safety of Technetium (99m Tc) Fanolesomab in patients with abnormal polymorphonuclear leukocyte (PMN) counts who have equivocal signs and symptoms of appendicitis.

The study should

- Enroll patients who are candidates for Technetium (99m Tc) Fanolesomab imaging and have PMN counts at or below the lower limit of normal at the time of entry into the study
 - Compare the diagnosis of appendicitis by Technetium (99m Tc) Fanolesomab imaging with the final clinical diagnosis
 - Assess image quality
 - Be powered to detect at least a 25% relative worsening of the diagnostic performance of the product (based on sensitivity of 75%, sample size of 46 patients).
 - Collect data on all severe and/or serious adverse events. Collect data on all infections including response to antimicrobial therapy. .
 - Measure PMN counts before and after Technetium (99m Tc) Fanolesomab administration including following resolution of the acute event.
2. Please provide a commitment to conduct a dosimetry study in pediatric patients (5 to 16 years of age).
 3. To provide appropriate data supporting a validated, quantitative immunogenicity assay for the detection of an immune response (binding antibodies) to Technetium (99m Tc) Fanolesomab. The assay methodology and validation report will be submitted by _____.
 4. To provide data on immunogenicity of the product using the validated assay. If serum samples from clinical studies have been banked in a manner that would ensure stability of any anti-Fanolesomab response, these can be re-assayed using the revised assay method. The sample size should be sufficient to exclude incidence >10%.
 - Date of study completion: _____
 - Date of submission of final report: _____
 1. To conduct a study to determine the prevalence of interference of HAMA with diagnostic *in vitro* assays that use murine antibodies and to determine the relationship, if any, between interference and level of HAMA.
 - Date of study completion: _____
 - Date of submission of final report: _____
 2. To re-evaluate the in-process, release and shelf-life specifications for Fanolesomab Drug Substance, Intermediate Drug Product, and Drug Product

on a yearly basis to reflect increased manufacturing experience. The cumulative data and analysis for product manufactured up to and including 2004 will be provided in the July 2004 to July 2005 Annual Report to be submitted by September 30, 2005. Specifications will be re-evaluated on a yearly basis and the cumulative data and analysis for product manufactured up to and including 2010 will be provided annually.

3. To improve control of the HL-60 and Raji cells used in the potency assays by collecting stability data, validating new methods, and setting new specifications as specified below:
 - a. To develop and to validate a saturation binding method and evaluate the relationship between the numbers of binding sites as determined by saturation binding and the Lindmo method (IRF) values using a reference lot of antibody.
 - b. To establish acceptance specifications and an expiry period for the HL-60 and Raji cells that include limits for the number of binding sites/cell, and IRF values.
 - c. To submit updated protocols for qualification of new HL-60 and Raji cell banks based on information acquired from the above studies.

Validation reports, specifications and updated protocols will be submitted by _____. New HL-60 and Raji cell banks will be produced with the updated protocol.

4. To submit data validating the shipping of Fanolesomab samples for release testing to Palatin, including purified bulk drug substance and intermediate drug product from DSM Biologics in Groningen, The Netherlands to Palatin Technologies in Princeton New Jersey and of your drug product from Ben Venue Laboratories, Bedford, Ohio to Palatin Technologies in New Jersey. Additionally, data supporting your ability to maintain product at a temperature of 2-8°C when shipped from Ben Venue Laboratories to your distributor during elevated outside ambient temperatures (e.g. summer months) should be submitted for 3 separate shipments of NeutroSpec kits.
 - Date of study completion: _____
 - Date of submission of final report: _____
5. To submit drug substance, intermediate drug product, and drug product stability data for the Fanolesomab conformance lots for the requested expiration dating. For the Fanolesomab Drug Substance, Intermediate Drug Product, and Drug Product, please provide the following dates:

- Date of study completion: _____
 - Date of submission of final report: _____
6. To submit a post approval stability protocol for Fanolesomab. The protocol should identify situations when Fanolesomab will be put on stability, as well as include the following real time, long term stability studies:
- a. One drug substance lot manufactured per year for every year that drug substance is manufactured.
 - b. One intermediate drug product lot manufactured per year for every year that intermediate drug product is manufactured.
 - c. One drug product lot manufactured per year for every year that drug product is manufactured.

The protocol will be submitted by: _____

7. To submit the final validation report on the new Host Cell Protein Western blot assay currently being developed.

The report will be submitted by: _____

8. To perform genetic stability testing on a production lot of Fanolesomab at the limit of *in vitro* cell age. Peptide mapping results will be verified by comparing the nucleotide sequence of Fanolesomab in the master cell bank and in aged cells. The study will be completed by _____, and the final study report submitted by _____.
9. To develop and to validate assays and set quantitative limits for Fanolesomab carbohydrate composition prior to qualification of the next Fanolesomab reference standard. The study will be completed by _____, and the final study report submitted by _____.
10. To develop and to validate assays and set quantitative limits for IgM hexamer and J chain prior to qualification of the next Fanolesomab reference standard. The study will be completed by _____, and the final study report submitted by _____.

Please note that all clinical PMCs will require the following information. Please be specific regarding month/year for each of these.

Date of submission of final protocol
 Date of study initiation
 Date of study completion
 Date of submission of final report

Label Review Palatin Technologies STN 103928/0 - Technetium Tc 99m Fanolesomab

Dale Slavin, Ph.D. FDA, Regulatory Project Manager

(e-mail 3-25-04)

Dear Dr. Kaushik Dave and Dr. Dennis Earle,

This is an informal review of your carton and vial labels. This is not the final review, and other revisions may be requested.

General Comments

1. You will need to include your US license number on all your labels i.e., carton, vial, radioassay info label and package insert. Your license number will be 1588 this number is to be associated with your name and address and should immediately follow Palatin's address.
2. Please include on the carton and vial a "mock-up" of what both the expiration date and lot number will actually look like. FDA wants to know exactly how this will look to the physician and pharmacist (e.g., size, font character, embossed or printed).
3. Please include that you, Palatin, are the manufacturer on all labels.
4. As both the diluent vial and the fanolesomab vial are intended for single use please include the wording "single use vial" on both of these labels.
5. The bulk packaging of five fanolesomab vials and five diluent vials and five radioassay info tags and one package insert is problematic. Because of errors in packaging any one of these components may be left out. For safety reasons you should individually package a single kit (one fanolesomab vial, one diluent vial, one radioassay info tag and one package insert) in an individual kit carton; these individual kits may then be packaged in a multipack of five kits.
6. Please use the wording "For Intravenous Use" in place of (b) (4)

Specific Areas

Vial Label

7. LeuTech® should be the name of the Technetium Tc 99m Fanolesomab which is the final product. Thus the name of the vial should be Fanolesomab not LeuTech.
8. Please include the statement Protect from light.
9. The statement No preservatives should be included.

Drug Diluent Label

10. Please add single use vial
11. Please add for use in the preparation of LeuTech®.
12. Please explain why the 10 mg Sodium Hydrosulfite is so prominent.
13. Please remove the highlight from the Cenolate proprietary name.
14. Please include the lot and expiration date and define it as such.
15. Please include a storage statement and a protect from light statement. Although the ascorbic acid is in an amber bottle one would still not suggest leaving it in the light.

Radiolabeled Drug Information Tag

16. FDA strongly encourages you to make this secondary tag an adhesive tag not a string tag as you have indicated. If you wish to make this a string tag, FDA would want to know what is the rationale for why a string tag is necessary versus and adhesive tag.
17. Please indicate that this is a single use vial.
18. Please indicate what is in the vial i.e., vial contents.
19. Please include your name and address and US license #.
20. Please include the lot number and expiration date.

Carton

Panel 1 and Panel 2 (top and bottom)

No Text.

Panel 3

21. The US license number should be placed here.

Panel 4

22. FDA has concerns regarding the packaging of these five individual use kits in a bulk package with only one available package insert. It is very possible that there may be considerable lag between the imaging of the first patient with Tc 99m fanolesomab and the imaging of following four patients. LeuTech kit should be packaged individually with its own reaction vial, diluent, radiolabel info tag and package insert. These may then be packaged as a multipack of five separate kits.
23. Please ensure that contents are ordered with active ingredient first followed by largest to smallest amount of additive.

22 Pages of Draft Labeling have been Withheld in Full as b4
(CCI/TS) immediately following this page

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration
Center for Biologics Evaluation and Research

DATE January 31, 2001

FROM Mary Andrich, Bioresearch Monitoring
OCBQ/DIS
HFM-664

TO Chana Fuchs
Chair, BLA Committee
HFM-558

SUBJECT: Bioresearch Monitoring Inspection Results
BLA 99-1407
Product: 99mTc-LeuTech™ (Anti-CD 15 Antibody)
Sponsor: Palatin Technologies, Inc.

PROTOCOLS

98-004: An Open-Label, Multicenter Clinical Study to Evaluate the Efficacy and Safety of Technetium Tc 99m LeuTech™ Scintigraphy for the Detection of Appendicitis in Patients Presenting with Equivocal Signs and Symptoms

Blinded Read Methodology Report, Palatin Technologies Protocol 98-004, Tc-99m LeuTech™ Phase III Trial – Equivocal Appendicitis, BB-IND 7358

SUMMARY STATEMENT

The results of bioresearch monitoring inspections of two clinical sites and (b) (4) (b) (4) indicate that the submitted data, with the exceptions noted, is reliable.

BACKGROUND

Clinical investigator inspection assignments were conducted at two sites that performed studies in support of BLA 99-1407, and (b) (4). The inspections were conducted in accordance with CP 7348.811 (clinical investigator inspection program) and 7348.810 (CRO inspection program).

Data for subjects were taken from the BLA and compared to source data at the study sites. The assignment included specific questions about the studies. The following data audits were performed:

<u>Site/P.I.</u>	<u>FDA Form 483 Issued</u>	<u>Classification</u>
Sutter Roseville Medical Center/Weiland	No	NAI
Tri-City Medical Center/Kipper	Yes	VAI
(b) (4)	No	NAI

INSPECTIONAL FINDINGS

The inspection of Dr. Kipper revealed that he failed to calculate the pediatric dose correctly for seven subjects as follows:

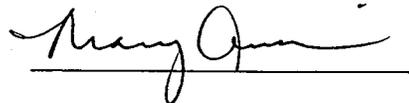
<u>Subject</u>	<u>Administered Dose (mCi)</u>	<u>Correct Dose (mCi)</u>
03	12	9
17	10	7.5
23	10.2	6.2
30	17.6	11.7
33	19.9	15.8
34	8	5.6
39	7	4.9

The inspections verified that the data reported in the BLA for these studies accurately represents the data in the source documents at the study sites.

BIMO ADMINISTRATIVE FOLLOW-UP

The inspection of Dr. Kipper was classified as VAI, and voluntary corrective actions were taken. The other inspections were classified as NAI.

Please contact me if you have any questions or seek additional information.



Mary Andrich

Attachment: FDA Form 483.

cc:

HFM-600
HFM-650 Cole
HFM-664 Salewski
HFM-664 Andrich
HFM-664 Access/Chron
HFM-664 BLA Summary File
HFM-99 BB IND-7358
HFM-99 BLA 99-1407
HFM-582 Robert Linblad
HFM-573 Lydia Martynec

HFR-CE150
HFR-CE150 Mike M. Rashti

HFR-PA100 Director
HFR-PA2565 Gerald McGirl
HFR-PA150 Rochelle B. Young

HFR-PA200
HFR-PA250 BIMO Coordinator
HFR-PA2535 Thomas R. Beilke

Memorandum

Food and Drug Administration
Center for Biologics Evaluation and Research
Office of Compliance and Biologics Quality
Division of Manufacturing and Product Quality

Date: August 31, 2000

To: Chana Fuchs, BLA Committee Chair, HFM-555

From: Deborah Trout, BLA Committee Member, HFM-675

Through: Julia Lukas, Branch Chief, HFM-675

Subject: Review of Biologics License Application (BLA) from Palatin Technologies for the manufacture, formulation, fill, lyophilization, and packaging of LeuTech™; STN Number 103928/0

My review includes an evaluation of the following sections submitted in Palatin's BLA application (reference is made to the table of Contents in Volume 1.1 of their submission dated November 22, 1999, STN number 103928/0: Volumes 1.3 (tabs 3.1, 3.4.1, 3.4.2, 3.4.3, 3.4.4, and 3.7), 1.4 (tabs 4.2.1 – 4.2.8, 4.3.1 – 4.3.8, 4.4, 4.5, and 4.7), 1.5 (tab 4.7), 1.6 (tab 4.7.6), 1.7 (tab 4.7.7), 1.8 (tabs 4.7.9 and 4.7.10), 1.10 (tabs 4.7.13 – 4.7.15, 4.8.1 – 4.8.4), 1.11 – 1.12 (tab 4.8.5), 1.13 (tab 4.8.6 and 4.8.7), and 1.14 (tabs 4.8.8 and 4.8.9).

This review memorandum is comprised of three sections. The first section are issues that can be addressed in an information request or complete review letter and the second section are issues that can be addressed in the pre-license inspection and the third section is my review narrative

Section I: Outstanding Issues

1. Outstanding inspectional issues identified on the FDA Form 483s dated March 21, 2000, issued at the conclusion of the pre-approval inspection of your contract manufacturer, Ben Venue Laboratories at their Bedford, Ohio location; May 5, 2000, issued at the conclusion of the pre-approval inspection of your contract manufacturer, DSM Biologics at their Groningen, Netherlands location; July 28, 2000, issued at the conclusion of the pre-approval inspection of your Edison, New Jersey location, have yet to be resolved.
2. Please submit process validation for the lyophilization method. The study should include data demonstrating that the following significant product attributes are consistently achieved

whenever the process is carried out as specified: (1) potency; (2) moisture content; (3) cake appearance for uniformity, shape and color; (4) reconstitution time and appearance; and (5) stability. Validation should include a minimum of three batches at target set points for pressure, temperature, and time. In addition, please submit complete lyophilization charts used to assess process validation product attributes.

3. Container Closure Integrity Testing Validation Study # PV-S14798M only assessed protection of the product from microbial contamination. Please submit your program for assessing final product container closure suitability for the following attributes: light protection, reactive gas permeation (b) (4) and compatibility of the elastomeric components.

4. Please submit validation data supporting the following RB5 intermediate hold times: (b) (4)

5. Please submit your procedures on how and when contract facilities will be periodically assessed for compliance with applicable product and establishment standards and cGMP.

6. Please submit written commitments from contract manufacturers stating all proposed changes to manufacturing and facilities, introduction of additional marketed products, and clinical material processing operations will be communicated to you prior to implementation. In addition, please submit your procedure for reporting changes to the Agency, as specified in 21 CFR 610.12.

7. Please submit written commitments from contract manufacturers stating you will be informed of all errors and deviations in manufacturing methods and test results, as well as adverse events, for the affected products.

Section II: Pre-license Inspection Issues

8. Volume 1.12, page 4-3040 "Manufacturing Process Validation for LeuTech at Ben Venue Laboratories" indicates that 2 lots were tested (0882-23-47413 and 0882-23-47414) for the validation study and the first commercial lot will be tested similarly to complete the three lot study. Please clarify if this lot has been produced and if not timelines should be submitted for production. In addition confirm that all equipment and assay validation was completed prior to process validation.

9. The residual moisture specifications for the lyophilized drug product is (b) (4) please review validation data supporting the specification.

10. Volume 1.13, page 4-3237 indicates that final product vial stoppers are (b) (4)
(b) (4) The submission indicates that the stoppers are (b) (4)
(b) (4) Please verify that Ben Venue has done some qualification of the stoppers (i.e.,

verification testing of endotoxin removal, one lot per year and verification of the (b) (4) process).

11. Volume 1.13, page 4-3258 states that final formulation of Leutech, at Ben Venue (b) (4) (b) (4) please review cleaning and sterilization validation for this container.

12. The Batch Product Record (BPR) states that the first 40 vials filled are designated as the (b) (4) test samples. Please verify that the product is (b) (4) (b) (4) (b) (4) is Ben Venue taking a representative bulk sterility sample?

13. Please review (b) (4) validation studies (extractable and bioburden) for the (b) (4) (b) (4) used to sterilize the LeuTech drug product.

14. Please clarify if the (b) (4) (b) (4) procedures.

15. Volume 1.13, page 4-3327 indicates that the fill line was down for mechanical reasons. In addition, Tray # 1 was rejected due to an exceed time limit (fill date 9-30-98). Please review the investigations for these deviations during the prelicense inspection.

16. The (b) (4) is sampled daily for cell count determination, viability (b) (4) and pH. (b) (4) The (b) (4) harvest bags are labeled with product description, lot number, article code, volume, label date, expiration date, storage temperature and status, and then sampled with a closed sampling device (Sterile Connection Device). Harvests are stored (b) (4) pending test results. Please review validation data for all closed systems and expirations dating for harvested material.

17. (b) (4)

(b) (4)

[REDACTED] (b) (4)

20. Volume 1.5, page 4-350 indicates that most classified areas, at the DSM facility, are monitored in the [REDACTED] (b) (4) Dynamic monitoring is dependent on the type of process. Please review monitoring frequencies and validation data for all classified areas.

21. Please review the cleaning validation for the following DSM equipment: [REDACTED] (b) (4)
[REDACTED] (b) (4)

22. During the prelicense inspection of the Ben Venue facility please review validation data for the [REDACTED] (b) (4)
Any one of these chambers may be used for Leulech lyophilization. The firm needs to ensure that the following parameters are validated and/or specified in detail with appropriate limits: shelf temperature control, including shelf temperature profile for entire freeze dry cycle; circulating fluid specifications; condenser temperature; refrigerant and specifications; system evacuation rates; vacuum integrity testing; sublimation rate/condenser capacity; condenser defrost time; sterilization; instruments and controls; and load size and configuration.

23. Please review cleaning validation for the [REDACTED] (b) (4) during the prelicense inspection.

[REDACTED] (b) (4)

25. The following disinfectants are used at the DSM facility: [REDACTED] (b) (4)
[REDACTED] (b) (4)

[REDACTED] (b) (4) All solution are prepared according to manufactures instructions and recorded in a logbook. Please review disinfectant effectiveness studies during the prelicense inspection.

26. The purified RB5 IgM drug substance is packaged in "tightly" sealed [REDACTED] (b) (4) [REDACTED] (b) (4) with screw caps and stored at [REDACTED] (b) (4) Please review container closure validation during the prelicense inspection.

27. Volume 1.4, page 4-78 indicates that stability studies have been implemented to assess the holding times of the intermediate RB5 products generated during manufacturing. At different production steps the process can be stopped and the intermediate can be stored at either room temperature [REDACTED] (b) (4) until further processing. The submission indicated that the stability of the following intermediates is currently being assessed, the harvest, concentrate, and eluates from the [REDACTED] (b) (4) Please review stability data

during the pre-approval inspection. In addition please review methods validation for assays used in the study.

28. Please review shipping validation for drug substance shipped from DSM to Ben Venue facility.

Section III: Review Narrative

Drug Product

LeuTech is a lyophilized formulation of a partially reduced mouse monoclonal IgM antibody. It is formulated with stannous ion, (b) (4), and excipients to permit subsequent radiolabeling with Sodium Pertechnetate Tc 99m, USP. The radiolabeled product is injected intravenously for diagnostic imaging of appendicitis.

The lyophilized Drug Product is manufactured at Ben Venue Laboratories by (b) (4)

(b) (4)

the ascorbic acid ampoule. The following is a list of in-process specifications and testing performed before (b) (4) by Ben Venue: Appearance (clear, colorless and free from visible contamination); Stannous Ion (for information only); UV assay (b) (4); (b) (4); pH (b) (4); Density (b) (4); and Bioburden (b) (4). In addition the following drug product release test are performed by Ben Venue;

Sterility (21 CFR 610.12); Particulate Matter (Light Obscuration Particle Count Test); and Bacterial Endotoxin (LAL).

(b) (4)



Kit Packaging

Packaging components: 3mL USP Type I glass, (b) (4), or equivalent and (b) (4), or equivalent. The outside packaging container is labeled with the appropriate lot number and expiration date reflecting the expiration date of the shortest dated component (LeuTech vial or Ascorbic Acid ampoule). The final kits are assembled to contain five LeuTech vials, five Ascorbic Acid Injection Diluent ampuls, and one package insert. Final packaged kits are maintained under quarantine status at 2° to 8°C until released for distribution.

Drug Substance

DSM Biologics provides contract manufacturing services for the drug substance (reduced RB5 IgM). (b) (4)

(b) (4) (b) (4) DSM manufacturers on a (b) (4)





(b) (4)



(b) (4)

cc: Fuch HFM-555 (electronic copy)
Epps HFM-594 (electronic copy)
Webber HFM-555 (electronic copy)
Noska HFM-588 (hard copy)