Food and Drug Administration
Center for Biologics Evaluation and Research
1401 Rockville Pike
Rockville MD 20852-1448

To: Administrative File: STN 125384/0

From: Lori Peters, Consumer Safety Officer, CBER/OCBQ/DMPQ/B1, HFM-676

Through: Carolyn Renshaw, Branch Chief, CBER/OCBQ/DMPQ/B1, HFM-675

CC: Yiping Jia, Chair, CBER/OBRR/DH/LBVB
Crystal Allard, RPM, CBER/OBRR
Deborah Trout, Team Lead, CBER/OCBQ/DMPQ/B1
Sean Byrd, Reviewer, CBER/OCBQ/DMPQ/B1

Applicant: Kedrion Biopharmaceuticals, S.p.A. **Facility Site**: Via Provinciale Bolognana, Gallicano (Lucca) Italy 55207

Product: 25% Human Albumin Solution, KEDBUMIN

Indications: Hypovolemia, Hypoalbuminemia, Prevention of Central Volume Depletion, Ovarian Hyperstimulation Syndrome, Adult Respiratory Distress Syndrome, Burns, Hemodialysis, and Cardiopulmonary Bypass Procedure

Subject: First Cycle Review Memo: Original BLA for 25% Human Albumin Solution, KEDBUMIN

Due Date: June 3, 2011

Summary

FFF Enterprises, Inc., submitted the BLA for the 25% Human Albumin Solution, KEDBUMIN, on behalf of the manufacturer, Kedrion Biopharmaceuticals, S.p.A., hereafter referred to as Kedrion. The BLA for 25% Human Albumin Solution was the first application submitted by Kedrion to the Agency for product licensure. The submission was appropriately filed as a BLA according to 21 CFR 601.2.

The submission was received by CBER on August 2, 2010 via paper format with electronic content consisting of 5 volumes divided into 5 modules. DMPQ reviewed the following BLA modules:

- Module 1: Administrative Information

    - Section 1.1: Forms
    - Section 1.2: Cover Letter
    - Section 1.3: Administrative Information
    - Section 1.4: References
    - Section 1.6 Meetings
    - Section 1.12 Environmental Analysis
- Module 2: Common Technical Document Summaries
    - Section 2.2 Introduction
    - Section 2.3 Quality Overall Summary – Drug Substance Introduction
    - Section 2.3.S.1 General Information
    - Section 2.3.S.2 Manufacture
    - Section 2.3.S.4 Control of Drug Substance
    - Section 2.3.S.5 Reference Standards or Materials
    - Section 2.3.S.6 Container Closure System
    - Section 2.3.P Quality Overall Summary – Drug Product
    - Section 2.3.P.1 Description and Composition of the Drug Product
    - Section 2.3.P.2 Pharmaceutical Development
    - Section 2.3.P.3 Manufacture
    - Section 2.3.P.4 Control of Excipients
    - Section 2.3.P.5 Control of Drug Product
    - Section 2.3.P.7 Container Closure System
    - Section 2.3.A Quality Overall Summary – Appendices
    - Section 2.3.A.1 Facilities and Equipment
    - Section 2.3.R Quality Overall Summary – Regional Information
- Module 3: Quality
    - Section 3.2.S Drug Substance Introduction
    - Section 3.2.S.1 General Information
    - Section 3.2.S.2 Manufacture
    - Section 3.2.S.4 Control of Drug Substance
    - Section 3.2.S.6 Container Closure System
    - Section 3.2.P Drug Product Introduction
    - Section 3.2.P.1 Description and Composition of the Drug Product
    - Section 3.2.P.2 Pharmaceutical Development
    - Section 3.2.P.3 Manufacture
    - Section 3.2.P.5 Control of Drug Product
    - Section 3.2.P.6 Reference Standards or Materials
    - Section 3.2.P.7 Container Closure System
    - Section 3.2.A Appendices
    - Section 3.2.A.1 Facilities and Equipment
    - Section 3.2.R Regional Information
    - Section 3.2.R.2 Comparability Protocol

An Information Request from DMPQ was sent to Kedrion on May 26, 2011 with responses received by CBER on May 31, 2011; Amendment No. 26. The responses required clarification and a teleconference

was held with Kedrion on May 31, 2011. The meeting minutes from the teleconference are documented in a separate memo. During the teleconference, Kedrion agreed to 1 post-marketing commitment (PMC) regarding ----------(b)(4)----------. The PMC was sent in a separate amendment to the BLA; Amendment No. 27. Following the teleconference, Kedrion responded with additional information regarding ----------(b)(4)----------, Amendment No. 28.

An inspection of Kedrion was performed on 23 – 25, 28 February 2011; 1 – 2 March 2011 and the observations are documented in the Establishment Inspection Report (EIR). A 4-item FDA Form 483 was issued to Kedrion. Responses to the FDA Form 483 are documented in a separate memo.

The scope of my review is primarily based on The Guidance for Industry*, Sterile Drug Products Produced by Aseptic Processing – Current Good Manufacturing Practice*, (CBER) September 2004; and the Biologics Regulations.

Reviewer Recommendation: Recommend Approval for the BLA with the following post-marketing commitment, outlined below; and a limited number of inspectional follow-up items for Team Biologics which are outlined in a separate memo.

Post-Marketing Commitment:

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Introduction

Kedrion is seeking their first US FDA Licensure specifically for the 25% Human Albumin Solution, KEDBUMIN. Kedrion has manufactured Albumin solution (market name: UMAN ALBUMIN) since 1968 and the product is sold in 41 countries throughout Europe, Asia, South America, and the Middle East. In addition to the Human Albumin Solution, Kedrion also manufactures immunoglobulin, coagulation factor, and plasma derivate products.

The manufacturing facility for the Albumin product is located at Via Provinciale; Bolognana, Gallicano (Lucca); Italy 55027. Kedrion has a second manufacturing facility in Naples, Italy but all manufacturing related to the Albumin product is completed at the facility in Bolognana. The inspection performed by DMPQ and OBRR members was performed at the production facility in Bolognana and the warehouse located in Castelvecchio Pascoli, Italy. Three conformance lots, ----------(b)(4)---------- were manufactured of the 25% Human Albumin Solution; the manufacturing description and test results for the lots were provided in the BLA.

Kedrion purchases the albumin paste intermediate from ----------(b)(4)----------, and further manufactures the paste into the final Albumin solution

product. The raw material for the paste is obtained from source plasma that is collected in licensed US plasmapheresis centers in accordance with US and EU regulations. The manufacturing process from the plasma pool to the production of the albumin paste is completed ----(b)(4)---; this process was licensed under -----(b)(4)----- and was not reviewed under this BLA for Kedrion. An inspection --(b)(4)--- was waived.

Environmental Assessment (Exclusion)

Kedrion claims categorical exclusion to the requirement for filing an Environmental Impact Analysis Report for KEDBUMIN based on 21 CFR 25.31c. A categorical exclusion memo was approved by CBER as part of the BLA.

Product Indications

Kedrion has identified the following eight indications for the 25% Human Albumin Solution:

- Hypovolemia – Restoration and maintenance of circulating blood volume where volume deficiency is demonstrated and colloid use is appropriate.
- Hypoalbuminemia – When the albumin deficit is the result of excessive protein loss, the effect of albumin administration will be temporary unless the underlying disorder is reversed.
- Prevention of Central Volume Depletion – Specifically after paracentesis due to cirrhotic ascites.
- Ovarian Hyperstimulation Syndrome
- Adult Respiratory Distress Syndrome
- Burns
- Hemodialysis – For patients undergoing long term dialysis or for those patients who are fluid-overloaded and cannot tolerate substantial volumes of salt solution for therapy of shock or hypotension.
- Cardiopulmonary Bypass Procedure – As part of the priming fluid.

Product Description

KEDBUMIN is a clear slightly viscous liquid, almost colorless, yellow, amber or green, obtained from human plasma. The 25% Human Albumin Solution, intended for intravenous administration, is a liquid sterile preparation containing 25% protein of which not less than 96% is albumin. KEDBUMIN is aseptically filled into 50 mL glass vials.

Manufacturing Process Description

Due to the continuous manufacturing process of KEDBUMIN, prior to the final formulation steps, ----------(b)(4)----------.

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Reviewer Comment: Additional information related to the raw materials acceptance activities and vendor qualification can be referenced in the EIR, Section 9.1 "Raw Materials Receipt, Quarantine, Storage, and Distribution", and Section 9.2 "Vendor and Supplier Qualification".

Manufacturing Description

The manufacturing flow chart for the production of the Albumin bulk is seen in Figure 1. A description of the albumin bulk process, divided into phases, follows Figure 1.

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Albumin Drug Product

The manufacturing steps in which the Albumin bulk is processed into the final drug product are: ----------(b)(4)----------, and heat treatment of the filled containers as a viral inactivation step.

Product Composition

The composition of the Albumin product along with a description on the content and reference standard is summarized in Table 2.

Table 2: Composition of the 25% Human Albumin Solution Product

Albumin Product Ingredient	Content	Function	Reference Standard
Active Pharmaceutical Ingredient (API): Human plasma proteins containing at least 96% albumin	12.5 g	API	21 CFR 640.80 – 84 -----(b)(4)---------- Albumin (human)
Excipients: Sodium caprylate, 20 mmol/L	0.166 g	Stabilizer	----------(b)(4)----------
N-Acetyl-DL-Tryptophan, 20 mmol/L	(b)(4) g	Stabilizer	------(b)(4)---------
Other Ingredients: WFI	50 g	Solvent media	----------(b)(4)----------
Total Na+ Concentration	--(b)(4)--		

Two excipients, Sodium caprylate and N-Acetyl-DL-Tryptophan, are added in amounts that are proportional to the protein content of the bulk solutions (0.08 mmol per gram of protein). This concentration has been shown to guarantee that albumin in solution is stable during the heat treatment step of the final filled product. This formulation is commonly used for therapeutic albumin preparations and complies with 21 CFR 640.81(f).

The quality of the excipients is guaranteed by the certificates of analysis provided by the supplier and by the controls performed at Kedrion in accordance with -------------(b)(4)---------------. The excipients are tested for ---(b)(4)--- as part of the incoming testing activity. The results from the ---(b)(4)--- testing on the excipients were provided in the BLA, Module 2.3.P.4. The data were reviewed and met the criteria.

Manufacturing Description

The manufacturing flow chart for the production of the 25% Human Albumin Solution product is seen in Figure 2. A description of the production process, divided into phases, follows Figure 2.

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Reviewer Comment: The aseptic filling of the albumin bulk into the final containers and the environmental monitoring controls were both witnessed during the inspection; for additional details reference EIR, Section 7.1 "Production Operations Observed".

Phase B: Heat Treatment (Viral Inactivation), Labeling and Packaging
Heat treatment of filled and closed glass vials is performed within 24 hours after filling with the temperature/time conditions of 60°C ± 0.5°C maintained for 10 - 11 hours in accordance with 21 CFR 640.81. Autoclave -(b)(4)- is used for the heat treatment of the bottles. Following heat treatment, the vials are incubated at --(b)(4)-- for at least 14 days according to 21 CFR 640.81. The vials, after incubation, are stored at a temperature not exceeding 30°C awaiting final packaging.

All vials are inspected for transparency, particles, and color variability by an automatic visual inspection machine. The vials rejected by the machine are evaluated by qualified operators. The conforming vials are directly labeled and packaged. Each box contains 1 product vials and 1 product information insert. During packaging, samples are taken at pre-defined intervals to verify the correctness and completeness of the mobile data (batch number and expiration date) and the presence of the package components. Archival samples are withdrawn at the end of packaging.

The final product is stored in quarantine areas at a temperature not exceeding 30°C, according to product specifications.

Reviewer Comment: As originally reported in the BLA, Kedrion performed a 100% automatic visual inspection and a manual inspection of the vials that were rejected by the automatic inspection machine. During the inspection, the inspectors noted that Kedrion is not performing an adequate visual inspection of the vials as they do not check for cracks or particulates lodged in the neck region of the vial. These observations were listed on FDA Form 483, Item #1. In response to the 483, Kedrion will perform only a manual visual inspection of the vials of KEDBUMIN filled for the US market and will inspect for particulate in the neck region and cracks. The inspectors concur with Kedrion's response to the visual inspection observation and consider the observation resolved. For additional details, reference EIR, Section 8.10 "Equipment Qualifications - Visual Inspection" and the Review of 483 Response Memo.

Analytical Testing of the Final Product
The analytical tests that are performed on the final product are listed in Table 3 below.

Table 3: Analytical Tests for the Final Product

Test	Specification/Limit

Character	A slightly viscous liquid, it is almost colorless, yellow, amber or green
Total protein (g/L)	235 – 265
pH	6.4 – 7.4
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Identity	The main component of the preparation corresponds to main component of human serum
Protein composition (%)	≥ 96
Sodium (mEq/L or mmol/L)	130 – 160
Potassium (mEq/L or mmol/L)	≤ 2
Aluminum (ppb or µg/L)	≤ 200
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Sterility	Sterile
Pyrogens	Pyrogens free (----------(b)(4)----------)
Sodium caprylate (mmol/g proteins)	0.064 – 0.096
N-Acetyl-DL-tryptophan (mmol/g protein)	0.064 – 0.096
--------(b)(4)---------	(b)(4)
Heat Stability (50 hours/57°C)	Unchanged after 50 hour at 57°C
General Safety	----------(b)(4)---------- No unexpected response or weight loss in mice and guinea pigs after 7 days
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* Results are not reported on the CoA

The analytical test results from each of the conformance lots as listed in Table 3 were provided in the BLA in Module 2.3.P and in the process validation report, VPC-031-R-01, *VPC Final Summary: Process Validation Study Human Albumin 25% (US) Manufacturing Process*, Date: May 28, 2010. The test results from each conformance lot meet the criteria as confirmed in the review of Module 2.3 and Report VPC-031-R-01.

Analytical Test Method Validation

The analytical methods to test the finished product were validated by Kedrion. DMPQ reviewed the validations for the analytical test methods of Sterility, Bacterial Endotoxin, and Bioburden as provided in Module 3 of the BLA.

Sterility

The analytical method is performed in accordance to --(b)(4)-- Sterility Test, current edition. The membrane filtration technique is applied. Kedrion maintains SOP QCS-05-17 for Sterility Testing and the validation of the procedure is documented in MTA-052-R. A summary of the validation results from MTA-052-R follows.

The characteristics that were evaluated during the validation include:

- Culture media and incubation temperatures: The culture media must be fertile and promote the growth of the challenge micro-organisms within the time and temperatures required by ----------(b)(4)----------.
- Sterility of the product (bacteriostatic/fungistatic test): This test is to verify that the product to be analyzed has no antimicrobial activities that could inhibit the growth of eventual micro-organisms, causing false negative results. The culture media used for the validation tests are TSB medium (Tryptic Soy Broth) suitable for the aerobic bacteria and fungi, and FTM (fluid thioglycollate medium) for the detection of aerobic and anaerobic bacteria. The Bacteriostasis/fungistatic test was carried out for direct inoculum of slow growth Microbic Strains *(----------(b)(4)----------, Bacillus Subtilis* and ------*(b)(4)*------*)*. This test was performed on 20% Albumin Human Solution as this is the common concentration of the Albumin product produced by Kedrion; the concentration is not significant for this test and the results apply also to the 25% solution. The results and acceptance criteria are summarized in Table 4.

Table 4: Sterility Validation Test Results

Parameter	Acceptance Criteria	Results
Bacteriostatic/ fungistatic test	The microbial growth in the product and in the positive control must be comparable	In all tests carried out on the product the growth of each of the micro-organisms used is comparable to the growth in positive control. So the product does not present bacteriostatic or fungistatic activity.
	No microbial growth in negative control	No growth in all tested negative control.

The sterility test method is considered validated based upon the results of the testing.

Bacterial Endotoxin

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Reviewer Comment: The validation for the analytical test methods of Sterility, Endotoxin, and Bioburden are adequate to ensure the repeatability of the test and ensure the correct results.

Control of Critical Steps and Intermediates

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Reviewer Comment: Media fill procedures and the results of the media fills performed in 2010 and 2011 were reviewed during the inspection; refer to EIR Section 7.4 “Media Fills” for additional details.

Evaluation of Environmental Monitoring Conditions
To verify that classified areas are in accordance with 21 CFR 210-211 CGMP standards and the FDA Guidance for Industry: *"Sterile Drug Products Produced by Aseptic Processing Current Good Manufacturing Practice"*, Kedrion implemented a qualification and monitoring program to evaluate the efficiency of the air conditioning system and the quality of environmental parameters. The program includes the requirements for: initial qualification and periodic re-qualification, and routine controls.

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Viral Reduction and Inactivation

The following steps are documented as capable of reducing possible viral contamination in Albumin derived from human plasma:

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- Fractionation of Effluent I to Effluent II+III – -(b)(4)-
- Fractionation of Effluent IV-1 to Effluent IV-4 – -(b)(4)-

- Depth filtration of Fraction V suspension – -(b)(4)-
- Heat treatment of 25% Human Albumin Solution at 60°C for 10 hours – Kedrion

Viral validation studies for the fractionation steps are reported in ----------(b)(4)----------. The viral validation study related to the final heat treatment step performed by Kedrion is reported in the "Adventitious Agents Safety Evaluation".

Reviewer Comment: DMPQ defers the review of the viral reduction and adventitious agent's safety evaluation to the product office for review.

Heat treatment (pasteurization) of the final product (filled and capped in glass vials) is performed in autoclave, --(b)(4)-- at 60 ± 5°C, for 10-11 hrs. The autoclave is located in Room ----------
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Reviewer Comment: The results of the validation in Report AUT-201-PQ-02-R were reviewed during the inspection; reference EIR Section 8.10 "Equipment Qualifications – Pasteurization Autoclave" for additional information.

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Facility Description and Controls

The manufacturing facility for KEDBUMIN production is located at Via Provinciale, Bolognana, Gallicano (Lucca), Italy 55027. The production departments involved in the preparation of KEDBUMIN specifically, Albumin Purification and Filling Department, are located in Building (b)(4) of the facility. A

detailed description of manufacturing site including production departments, utility systems, and maintenance, is addressed in document SMF-02-10, *Kedrion Bolognana Plant Site Master File*.

Facility Layout
The layout of the Albumin purification department and filling department were provided in the BLA. The layouts highlighted the room numbers, area classifications, and equipment in each room. Also provided in the BLA were the material flow, personnel flow, albumin paste flow, product flow, and waste flow. The information in each of the layout and the flow diagrams was confirmed during the inspection and no issues are noted.

Water Systems
The production, use, and maintenance of the pharmaceutical grade water systems at the Bolognana facility along with the water trending data was reviewed during the inspection; reference EIR, Section 8.4 "Water Systems" and Section 8.5 "Water Trend Reports" for additional details. The Clean Steam system was also reviewed during the inspection and details can be referenced in the EIR, Section 8.6 "Clean Steam".

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Reviewer Comment: The qualification of the HVAC monitoring system, -(b)(4)-, was reviewed during the inspection; see EIR Section 8.15 “Computer Systems” for details. The maintenance of the HEPA filters was discussed during the inspection; see Section 8.3 “HVAC”.

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Container Closure for the Albumin Product
KEDBUMIN is filled in colorless (b)(4) glass vials containing 50 mL of product solution. The (b)(4) stoppers are made of an ----------(b)(4)--------- rubber, 32 mm in diameter. The stoppers are secured by an aluminum overseal and a plastic flip-off top-cap.

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The glass vials are -------(b)(4)---------- glass, 50 mL volume size. The specifications of the bottle are as follows: body external diameter 46.0 (b)(4) mm, collar external diameter 32.0 (b)(4) mm, external diameter of neck 29.0 mm max, collar internal diameter 22.5 (b)(4) mm, and total height 68.0 (b)(4) mm. (b)(4) glass containers are used because (b)(4) glass has been shown to release a lower quantity of aluminum into Albumin products than (b)(4) glass.

The rubber closure stoppers are ---------(b)(4)---------- compound ----------(b)(4)----------. The specifications of the 32 mm stopper are the following: external diameter of the top 31.00 (b)(4) mm, external diameter of neck 24.20 (b)(4) mm, height of top 5.00 (b)(4) mm, and total height 16.00 (b)(4) mm. ---
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Chemical and physical quality control tests for final batch approval are performed according to SOPs in compliance with ----------(b)(4)----------, current edition. As part of the routine acceptance activities for the glass vials and stoppers, Kedrion will perform a dimensional analysis and chemical analysis along with a review of the CoA for both the glass vials and stoppers. The procedures for the controls on the glass vials and stoppers were provided in the BLA and reviewed. Synopses on each control document follows.

Kedrion maintains SOP QSP-05-51, *Controls on Glass Bottles*, Rev. 08, Effective Date: September 14, 2009, which describes the visual inspection tests and dimensional analysis tests that are to be performed on the glass vials as part of the acceptance testing. The operators will check for cleanliness of the vials, cuts, cracks, blisters, filaments, scratches, etc. in the glass as part of the visual inspection. For the dimensional analysis, the operators will measure the body diameter, external mouth diameter, internal mouth diameter, and total vial height.

Kedrion maintains SOP QSP-05-52, *Controls on ---(b)(4)--- Stoppers*, Rev. 05, Effective Date: March 3, 2008, which describes the visual inspection tests and dimensional analysis tests that are to be performed on the stoppers as part of the acceptance testing. The operators will check the surface of the stoppers; ensure the stoppers are free of cavities, cuts, lines, or other anomalies; ensure no foreign material (i.e. hairs, dust, dirt) are present; and the color is uniform and streak free as part of the visual inspection process. For the dimensional analysis, the operators will measure the tail piece diameter, head diameter, total height, and head height.

Reviewer Comment: The results of the dimensional analysis testing were reviewed during the inspection. The chemical analysis testing that is performed on the vials and stoppers was reviewed during the inspection; reference EIR, Section 9.5 “Container Closure” for details.

Validation of the Container Closure System

The integrity of the container closure system was evaluated by Kedrion for the following:

- Protection and Safety: Micro leak testing performed on representative samples for each batch, applied to the container-closure systems together with validated manufacturing procedures, prevents external contamination.
- Compatibility: No interaction with the product due to adsorption or degradation and no change in pH values have been demonstrated during the shelf life period. The stability data covering a period of 24 months for one batch and 12 months for other batches demonstrate no significant changes in pH, protein composition (albumin ~ 96%) and ----------(b)(4)----------.
- Safety: The choice of a (b)(4) glass container guarantees low aluminum content in the product at the end of the shelf life and testing has shown that this aluminum content is lower than 200 ppb, fulfilling current (b)(4) specifications.

Reviewer Comment: In the information request, Kedrion confirmed that the --------(b)(4)-------- as performed by the manufacturers were not assessed and ---(b)(4)--- were not performed. Kedrion agreed to review ----------(b)(4)----------; the assessment will be submitted in a PMC.

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Reviewer Comment: During the inspection, the DMPQ inspectors learned Kedrion verifies the integrity of the vials through the use of a -------(b)(4)------ which uses -----(b)(4)---- to test the integrity. DMPQ Inspector reviewed the qualification of the -----(b)(4)------ and the procedures for testing the integrity with the machine and recommended Kedrion replace the ----------(b)(4)---------- using ---*(b)(4)*--- with the -----(b)(4)----- method. The information related to the container closure testing and qualification of the -------(b)(4)------ are documented in the EIR, Section 8.10 "Equipment Qualification – Container Closure Integrity".

Prevention of Cross-Contamination and Product Mix-Up

Production of KEDBUMIN is by campaign basis only. Line clearance is performed prior to the start of manufacture. Disposable devices and utensils are used where possible to prevent cross contamination. The Albumin filling occurs in a dedicated suite separate from the other non-albumin products produced by Kedrion at the Bolognana facility, however, filling of UMAN ALBUMIN and KEDBUMIN do occur on the same filling line. Kedrion has separate filling needles and tubing for the EU and US products.

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Reviewer Comment: Final review of the adequacy of the (b)(4) cleaning cycle to remove (b)(4) was deferred to the product office (Division of Hematology) as DMPQ is not the subject matter expert regarding (b)(4) removal. The conclusions summarized above were noted on the information based in the literature. Based upon the review of the (b)(4) cleaning cycle by the responsible persons in the Division of Hematology, it can be determined from the Division of Hematology's response that the cleaning cycle is adequate to remove (b)(4).

Stability

A stability study is being performed by Kedrion to verify that KEDBUMIN maintains its physico-chemical and biological characteristics for a period of three years when stored at a temperature of 30 (b)(4)°C. The study includes an accelerated stability and a long-term stability program. For stability testing, (b)(4) batches of albumin paste from -(b)(4)- were further processed by Kedrion to obtain three batches of 25% Human Albumin Solution. Table 14 summarizes the lot number information for the paste and product placed on stability.

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Reviewer Comment: The stability program protocols and stability test results were deferred to the

product office for review.

Shipping Validation

The shipping validation of the paste from -(b)(4)- facility to Kedrion's facility in Bolognana was reviewed during the inspection; reference EIR Section 9.6 "Shipping Validation" for details.

References

- 21 CFR 600's – Biologics
- 21 CFR §211 – Current Good Manufacturing Practice for Finished Pharmaceuticals
- The Guidance for Industry*, Sterile Drug Products Produced by Aseptic Processing – Current Good Manufacturing Practice*, (CBER) September 2004

Review History

Date Prepared: LP, May 24, 2011
Date Commented: CR, May 25, 2011
Date Revised: LP, May 25, 2011; LP, June 1, 2011; LP June 2, 2011