Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Biologics Evaluation and Research
Division of Manufacturing and Product Quality

MEMORANDUM

Recommendation to Waive Pre-Approval Inspection

Date:	February 17, 2011
From:	Lori Peters, Consumer Safety Officer, OCBQ/DMPQ/MRB1
To:	BLA File – STN 125384/0
Subject:	Recommendation to waive the Biologics License Application pre-approval inspection for the manufacture of the albumin paste intermediate ----------(b)(4)----------, which is used in the manufacture of KEDBUMIN, a 25% Human Albumin Solution, at Kedrion S.p.A.
Through:	Carolyn Renshaw, Branch Chief, OCBQ/DMPQ/MRB1
Cc:	Crystal Allard, RPM, OBRR

Concurrent Clearance Routing

John A. Eltermann, Jr., R.Ph., M.S. Date
Director, Division of Manufacturing and Product Quality
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research

CONCUR

DO NOT CONCUR

Basil Golding, Ph.D. Date
Director, Division of Hematology
Office of Blood Research and Review
Center for Biologics Evaluation and Research

CONCUR

DO NOT CONCUR

Yiping Jia, Ph.D. Date CONCUR
BLA Chair
Division of Hematology
Office of Blood Research and Review
Center for Biologics Evaluation and Research DO NOT CONCUR

Summary: This memorandum recommends that the BLA STN 125384 pre-approval inspection be waived ----------(b)(4)---------- for the manufacture of the albumin paste intermediate used in the manufacture of KEDBUMIN, a 25% Human Albumin solution, manufactured by Kedrion S.p.A. in Bolognana, Italy.

Brief History: Kedrion S.p.A. (hereafter referred to as Kedrion) submitted the BLA for KEDBUMIN, 25% Human Albumin Solution (STN 125384). Kedrion has identified eight indications for the KEDBUMIN product including: hypovolemia, hypoalbuminemia, prevention of central volume depletion, ovarian hyperstimulation syndrome, adult respiratory distress syndrome, burns, hemodialysis, and for cardiopulmonary bypass procedures. Kedrion purchases the albumin paste intermediate product from -(b)(4)--, a US licensed manufacturer of human plasma products. ----------(b)(4)---------- where the albumin paste is manufactured, is a FDA licensed facility, License No. (b)(4), and has been inspected ---(b)(4) ----- in the past two years. The albumin paste intermediate has been manufactured --(b)(4)-- since 2002.

----------(b)(4)----------:

- ----------(b)(4)----------
- ----------(b)(4)----------
- ----------(b)(4)----------
- ----------(b)(4)----------
- ----------(b)(4)----------
- ----------(b)(4)----------
- ----------(b)(4)----------
- ----------(b)(4)----------
- ----------(b)(4)----------
- ----------(b)(4)----------

- ----------(b)(4)----------
- ----------(b)(4)----------

Basis for the Waiver:

This waiver is based on criteria outlined in the Centerwide SOPP 8410 “Determining When Pre-Licensing/Pre-Approval Inspections (PLI/PAI) are necessary.” As stated in the aforementioned SOPP, it is CBER’s policy that a pre-license or pre-approval inspection will generally be necessary for a BLA if any of the following criteria **in bold** are met:

The facility does not hold an active US license.

---(b)(4)--- currently holds CBER license (b)(4).

The facility has not been inspected in the last two years by the FDA.

--(b)(4)-- was inspected by the Agency less than two years ago. ----------(b)(4)---------- was most recently inspected ---------(b)(4)------, for the manufacture of ----------(b)(4)----------. The following provides a 2-year inspectional history of ---(b)(4)---; decision outcomes are all either Voluntary Action Indicated, or No Action Indicated (note that within this time period the subject firm/facilities were never assigned the status of Official Action Indicated):

----------(b)(4)----------

▪ ---------(b)(4)------	(b)(4)	(b)(4)	---(b)(4)---
▪ ---------(b)(4)-----	(b)(4)	(b)(4)	---(b)(4)---
▪ ---------(b)(4)-----	(b)(4)	---(b)(4)---	---(b)(4)---

The establishment is performing significant manufacturing step(s) in new (unlicensed) areas using different equipment (representing a process change). This would include areas that are currently dedicated areas that have not been approved as multi-product facilities/buildings/areas.

The manufacturing process of the albumin paste intermediate remains unchanged and manufacturing is not occurring in an unlicensed area of the --------(b)(4)----------.

The previous inspection revealed significant GMP deficiencies in areas related to the processes in the application/supplement (similar processes) or systemic

problems, such as QC/QA oversight.

The last inspection, conducted --------(b)(4)--------, was classified as Voluntary Action Indicated (VAI). No significant GMP deficiencies were found.

The manufacturing process is sufficiently different (new production methods), specialized equipment or facilities) from that of other approved products produced by the establishment.

The manufacturing process for albumin paste intermediate remains unchanged in this BLA.

Waiver Recommendation:
Based on the information provided in the BLA submission and the previous inspection reports supporting the overall compliance status of the license holder, the review committee recommends waiving the pre-approval inspection for the --(b)(4)-- facility associated with this BLA.