



**U.S. FOOD & DRUG**  
ADMINISTRATION

## Memorandum

**DATE:** August 10, 2018

**FROM:** Erin McDowell, Bioresearch Monitoring Branch  
Division of Inspections and Surveillance  
Office of Compliance and Biologics Quality

**THROUGH:** Dennis Cato, Branch Chief, Bioresearch Monitoring Branch  
  
Carrie M. Mampilly, M.P.H., Director, Division of Inspections and Surveillance

**TO:** Michael Kennedy, Ph.D., Chair/Primary Reviewer  
Leland Ross Pierce, M.D., Clinical reviewer  
Edward Thompson, RPM

**SUBJECT:** Bioresearch Monitoring Review Memo  
**APPLICANT:** Octapharma Pharmazeutika Produktionsges.m.b.H.  
**PRODUCT:** Immune Globulin Subcutaneous (Human) [CUTAQUIG]  
**BLA:** 125668/o

### Review Summary

Bioresearch Monitoring (BIMO) inspections were conducted at four clinical investigator study sites that participated in the conduct of Study SCGAM-01. The inspections did not reveal significant problems that impact the data submitted in support of this Biologics License Application (BLA).

### Background

Octapharma Pharmazeutika Produktionsges.m.b.H submitted this BLA to obtain a marketing approval for subcutaneous (SC) administration of Immune Globulin Subcutaneous (Human) [CUTAQUIG] for treatment of primary immunodeficiency (PID) in adults. The following study was conducted to support this BLA.

### **STUDY SCGAM-01**

*Clinical Phase 3 Study to Evaluate the Pharmacokinetics, Efficacy, Tolerability and Safety of Subcutaneous Human Immunoglobulin ((b) (4) 16.5%) in Patients with Primary Immunodeficiency Diseases*

This study was conducted at 18 sites globally. Three domestic and one foreign sites were inspected in support of this BLA. The inspections were performed in accordance with FDA's Compliance Program Guidance Manual (CPGM) 7348.811, Inspection Program for Clinical

Investigators. Information submitted in the BLA was compared to source documents at each clinical study site. The BIMO inspection assignment also included specific questions concerning Study SCGAM-01. There were 61 subjects enrolled in the study. Random data was reviewed for 21 subjects, which represented approximately 34% of the enrolled subjects.

### Noteworthy Inspection Findings

BIMO Inspections were conducted at the following clinical sites:

Site ID	# of Subjects	Study Site	Location	483 Issued	Final Inspection Classification
11	4	Faculty Hospital by St. Anna in Brno	Czech Republic	Yes	VAI
42	5	University of California-Irvine	Irvine, California	Yes	VAI
43	5	Toledo Institute of Clinical Research	Toledo, Ohio	Yes	NAI
47	7	Pediatric Pulmonary Associates of North Texas	Frisco, Texas	Yes	VAI

NAI = No Action Indicated; VAI Voluntary Action Indicated

No significant inspectional findings were identified. Each of the sites inspected were issued a FDA Form 483.

A review of the inspection report and 483 for Site#11 revealed that the site used the incorrect body weight data for initial dose calculations, failing to recalculate dose when subject body weight changed by 5%, and neglecting to perform and review inclusion laboratory tests. This inspection was classified as Voluntary Action Indicated (VAI).

A review of the inspection report and 483 for Site#42 revealed four subjects were dosed using the incorrect infusion rate for the first 6 administrations, temperature logs were not created until 8 months after collection of specimens, and one subject received a forbidden concomitant medication for over 30 days. This inspection was classified as VAI.

A Form FDA 483 was issued to Site#43 at close of inspection for missing financial disclosure information. The site provided the documentation after the inspection was completed. This inspection was classified as No Action Indicated (NAI).

A review of the inspection report and 483 for Site#47 revealed a serious adverse event was not reported to the sponsor within 24 hours as required by the protocol; one subject received a concomitant medication at a dosage prohibited by the protocol that was not reported as a deviation; and several procedures required by the protocol were not performed. This inspection was classified as VAI.

### Sponsor/Monitoring Issues

No sponsor or monitoring issues were identified during the clinical site inspections.

Financial Disclosure

The Clinical Investigator Compliance Program directs the FDA investigator to ask the clinical investigator if and when he/she disclosed information about his/her financial interests to the sponsor and/or interests of any sub-investigators, spouse(s) and dependent children, including if and when the information was updated. The information submitted to the BLA was verified for each of the inspected clinical sites.

Administrative Follow-up:

Information letters were issued to the clinical investigators at all inspected sites.

Should you have any questions or comments about the contents of this memo or any aspect of BIMO, please contact me at 240-402-9014.

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Consumer Safety Officer

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EDR 125668/0 Application Folder  
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