DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
158-15 Liberty Avenue Jamaica, New York 11433 (718) 662-5586	23 - 31 March 2010
	FEI NUMBER 1000514603

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Daniel P. Van Plew, Senior Vice President & Manager

FIRM NAME	STREET ADDRESS
Regeneron Pharmaceuticals, Inc.	81 Columbia Turnpike
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Rensselaer, New York 12144	Biotechnology Drug Manufacturer

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DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

1. Following a number of failing "clean hold validation studies" for multiple equipments based on bioburden/ endotoxin results which did not meet acceptance criteria and which were concluded to be related to the WFI supply to those specific equipments:

• The firm failed to conduct a comprehensive investigation of the WFI system in building b(4) to determine the root cause/ source.

• The firm enlisted the services of a contract firm to conduct a sanitization and passivation of the system, however, there was no comprehensive investigation to examine system design, work order histories and other system related information which may have identified contributing factor(s)/ underlying cause of the WFI-related failures.

2. There are no security measures employed in the issuance of worksheets in the raw material testing laboratory located in building b(4) Inspection found that it is possible to print additional uncontrolled blank worksheets.

3. Review of the firm's manual log for SCARs (Supplier Corrective Action Requests) which was stated to be the original, GMP document for tracking these events found numerous entries for the past two years which were not closed out. This log is used for tracking of potential quality issues related to raw materials received from vendors.

4. The firm's written procedure SOP GE515 "Investigation and handling of out-of-specification (OOS) and Atypical Test Results" fails to provide adequate instruction regarding the follow-up to stability test failures for marketed product. In section 7.3.1.3 the document states "Investigations related to unexpected stability failures may need additional time to complete in order to obtain data on b(4)

5. The role of the "reimbursement vendor" in providing information related to quality complaints and the documentation in the complaint file of communications with that agent is not adequately addressed in the applicable complaint handling procedure. With regard to the latter point, it is noted:

• The two separate investigation reports for two groupings of complaints concerning lack of effectiveness (complaints 08-004, 08-005, 08-006, 08-007, 08-008 and 08-009, 08-010, 08-011) include statements regarding information reported to have come from the reimbursement vendor which pertained directly to a critical component in the final evaluation of these complaints, i.e., patient non-compliance.

• The complaint file does not identify the individuals involved in the communication, other details or supporting documentation for that conclusion.

• Interview of AERs personnel from the firm's pharmacovigilance office in Tarrytown, NY and review of reports of adverse events from the same time period which were received separately by the pharmacovigilance group at that office found no evidence of reports of non-compliance.

6. Quality Assurance review of data included in the report of investigation follow-up to complaints 08-009, 08-010 and 08-011of lack of efficacy for Arcalyst, lot B070012A was inadequate in that it failed to detect that the peptide mapping profiles of fully glycosylated and deglycosylated rilanocept show no significant differences in the retention times or peak heights. The peptide maps were conducted to compare primary structure of the complaint lot and the clinical lo b(4)

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	Robert C. Horan Chad M. Thompson	Robert C. Horan, Ph.D., Investigator Chad N. Thompson, Investigator	31 March 2010