DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
10 Waterview Blvd., 3rd Floor Parsippany, NJ 07054 (973)331-4990 Industry Information: www.fda.gov/oc/industry	3/28,29,30/12; 4/2,3,4,11,16/12
	FEI NUMBER 2243092

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Dr. David P. Jacobus, President

FIRM NAME	STREET ADDRESS
Jacobus Pharmaceuticals Company, Inc.	Industrial Research Laboratory Building, Schalks Crossing Road
CITY, STATE AND ZIP CODE Plainsboro, NJ 08536	TYPE OF ESTABLISHMENT INSPECTED Active Pharmaceutical Ingredient & Finished Dosage Manufacturer

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

QUALITY SYSTEM

OBSERVATION 1

There is a failure to thoroughly investigate batches that do not meet specification.

A. There was a failure to request a manufacturing investigation from a contract manufacturer after one drum of Lot #1437 of 4-Aminosalicyclic Acid USP, an Active Pharmaceutical Ingredient (API), failed specification for moisture content (spec: (b) (4) result: 1.094% KF). There is no investigation to determine: root-cause, if other segments of the lot were impacted, and whether corrective actions were identified to prevent reoccurrence. The remainder of the lot continued processing and was incorporated into Lot #14269 of PASER granules.

B. There is a failure to properly evaluate other batches of a drug product that may be adversely impacted following the failure of a batch to meet specification. An investigation into the failure of Lot #14028 of uncoated PASER granules for dried, sifted in-process (b) (4) test (i.e. particle size of the granules) determined variability in (b) (4) Lot #3614J as the root cause. Lot #14032 and #14045 of uncoated PASER granules were aborted at the extrusion step due to atypically large granules. Lot #14029 of uncoated PASER granules containing (b) (4) Lot #3614J was permitted to finish processing. The investigation failed to include an impact of assessment for evaluating if other batches of uncoated PASER granules utilizing (b) (4) Lot #3614J were impacted.

FACILITIES AND EQUIPMENT SYSTEM

OBSERVATION 2

Procedures for cleaning equipment used during the manufacturer of active pharmaceutical ingredients are not followed.

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	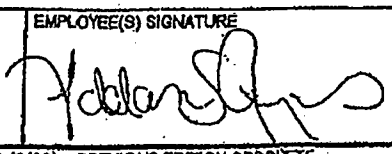	Addam S. Reynolds, Investigator	4/16/2012

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Specifically, there is not a requirement for the visual assessment of cleanliness of all equipment used in the manufacturer of 4-Aminosalicyclic Acid USP. Procedure, G-0018-01, Equipment Cleaning in General, dated 1/7/2004 requires all equipment to be visually inspected for cleanliness prior to use and requires the inspection to be documented in the batch record. The following was observed:

A. On 4/3/2012, I observed excessive white residue in dissolution tank JPC #(b) (4) used in the manufacturer of 4-Aminosalicyclic Acid USP. The manufacturing record for Lot #1481 of 4-Aminosalicyclic Acid USP indicated that the vessel was rinsed (cleaned) with purified water on 3/29/2012. A visual assessment of cleanliness prior to use is not documented in the batch record.

B. On 4/3/2012, I observed what appeared to be a brown residue in (b) (4) Kettle JPC (b) (4) used in the manufacturer of 4-Aminosalicyclic Acid USP. The manufacturing record for Lot #1481 of 4-Aminosalicyclic Acid USP indicated that the vessel was rinsed (cleaned) with purified water on 3/29/2012. I noted that an adequate visual assessment of cleanliness of the vessel is not possible for this piece of equipment as the viewing window appeared to be scratched making the inside of the vessel difficult to clearly observe. A visual assessment of cleanliness prior to use is not documented in the batch record.

OBSERVATION 3

Facilities used in the manufacture and storage of components, active pharmaceutical ingredients, and in-process materials are inadequate.

A. There is no temperature mapping study for the cold-storage room in the auxillary facility, located on the premises but separate from the main facility. The walls are lined with an insulating material that does not appear to facilitate cleaning. There is inadequate space to facilitate cleaning and inspection of containers and to prevent mix-ups. This warehouse is used to store uncoated PASER granules and 4-Aminosalicyclic Acid USP.

B. The ambient storage room in the auxiliary facility, located on the premises but separate from the main facility, is not maintained in a state of repair. There is a small hole (approximately 1 inch) in the posterior door; there is also a space between the floor and the bottom of the main door. I observed foliage in the warehouse. This

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warehouse is used to store technical grade Dapsone and Aminosalicylate Sodium BP.

C. Manufacturing Room (b) (4) is currently under construction. I observed an exposed wall, an HVAC line with duct tape, cardboard covering a vent in the room, and vents with a dust-like appearance. This room is used to store in-process, uncoated PASER granules.

D. The walls in the drying suite, used in the manufacturer of uncoated PASER granules, is not in a suitable state of repair. I observed several, small gouges (approximately 1 inch long) in the wall located within the suite.

E. The manufacturing area for Dapsone USP is not maintained in a state of repair. The ceiling in the area used in Dapsone precipitation and slurry washing has a hole (approximately 2 inches) in the plastic covering. The entrance to the suite is lined with a plastic sheet. In addition, I observed unidentified black residue on the floor adjacent to manufacturing vessels.

OBSERVATION 4

Equipment used in the manufacture of drug products are not maintained in a state of repair.

Specifically, (b) (4) used during milling of Dapsone USP in not maintained in a state of repair. I observed chipped paint on this piece of equipment. This piece of equipment was used during milling of Dapsone USP Lot #1470, Part I and II on 3/20/2012.

PRODUCTION SYSTEM

OBSERVATION 5

There is a lack of specific manufacturing instructions and control procedures.

A. The manufacturing process for the Active Pharmaceutical Ingredient (API) Dapsone USP includes a (b) (4) Dapsone slurry washing step, for the removal (b) (4) Step 53 in the master manufacturing record instructs operators to wash

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the slurry (b)(4) times with (b) (4) gallons of purified water. The following deficiencies were noted:

1. Dapsone USP is not routinely evaluated for residual (b) (4) to verify that the wash step reduces (b) (4) to an acceptable level.

2. The master manufacturing record fails to include adequate instructions for performing this (b) (4) operation to ensure consistency. Step 53 in the master manufacturing record instructs operators to wash (b)(4) times with (b) (4) gallons of purified water; however, instructions do not detail how this (b) (4) operation is performed by operators or when the slurry is determined to be adequately suspended.

3. Procedure G-0004.003, Personal Hygiene and Proper Dress, dated 3/3/2011, requires (b)(4) different gowning requirements for this step. It is not clear what are the correct gowning requirements for this step.

4. There is not an established procedure requiring operators to sanitize their gloved hands before (b) (4) mixing Dapsone slurry. In addition, gloves are reused and there is no procedure to detail: the cleaning of gloves, the requirements for when gloves can be reused or how used gloves are stored prior to additional use.

B. There is a failure to establish a final yield specification for Dapsone USP. A percent theoretical yield is calculated at the end of the manufacture of Dapsone USP; however, there is no specification for the final yield or provisions to require an investigation if the yield is atypical.

OBSERVATION 6

Containers used during the production of drug products are not identified at all times.

Specifically, during a walkthrough of the facility on 3/28/2012, I observed an orange container of in-process PASER without a label identifying the material. Lot #14563 (blend, in-process of being extruded) and #14569 (blend) of in-process PASER were being processed in Manufacturing Room (b)(4) during this time.

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LABORATORY CONTROL SYSTEM

OBSERVATION 7

The written stability program for drug products does not include specific, meaningful, and reliable test methods.

Specifically, the stability program for Dapsone 25 mg and 100 mg tablets does not include a stability-indicating method to monitor potential impurities. Test method (b) (4) Determination of Related Compounds in Dapsone Tablets: 25 mg and 100 mg, has been developed to evaluate impurities; the method is in draft and has not been validated for its intended use.

This is a repeat observation from the FDA-483 issued on 2/24/11.

OBSERVATION 8

Test results from component suppliers are accepted without testing each component according to the established specification without evaluating the reliability of the supplier's analyses.

Specifically, full testing for Nitrogen NF is not performed; an identity test is performed with all other testing accepted from the supplier's Certificate of Analysis (COA). There is no procedure for performing reduced testing to require an initial assessment of the reliability of the supplier's COA, and verification of the supplier's COA at appropriate intervals. Nitrogen NF is used during the commercial manufacture of (b) (4) (b) (4)

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