DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
International Compliance Team, DMPQ/OC/CDER, FDA White Oak Buiding 51, 4th Floor 10903 New Hampshire Avenue Silver Spring, MD 20993 USA (301) 827-8942 (ETB)	Feb. 20, 21, 22, 25 & 26, 2008 FEI NUMBER

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Mr. Yan Wang, General Manager

FIRM NAME	STREET ADDRESS
Changzhou SPL Company, Ltd	**3 Changhong West Road**
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Wujing, Changzhou City, Jiangsu Province, China	**API (animal origin) Manufacturer**

THIS DOCUMENT LISTS OBSERVATIONS MADE BY THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OF YOUR FACILITY. THEY ARE INSPECTIONAL OBSERVATIONS, AND DO NOT REPRESENT A FINAL AGENCY DETERMINATION REGARDING YOUR COMPLIANCE. IF YOU HAVE AN OBJECTION REGARDING AN OBSERVATION, OR HAVE IMPLEMENTED, OR PLAN TO IMPLEMENT, CORRECTIVE ACTION IN RESPONSE TO AN OBSERVATION, YOU MAY DISCUSS THE OBJECTION OR ACTION WITH THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OR SUBMIT THIS INFORMATION TO FDA AT THE ADDRESS ABOVE. IF YOU HAVE ANY QUESTIONS, PLEASE CONTACT FDA AT THE PHONE NUMBER AND ADDRESS ABOVE.

DURING AN INSPECTION OF YOUR FIRM we OBSERVED:

1. There have been no critical processing steps identified for the Heparin Sodium USP [ ] process, and, the repeated and efficient removal of impurities, such as proteins, nucleotides, virus, endotoxin, bacteria and heavy metals at the appropriate, specified, process steps has not been evaluated. There was no report for annual [ ] test results available.

The improvements offered by removal of a raw material [ ] test @ [ ] a batch size increase, an added [ ] step, a change in [ ] for the [ ] step and [ ] and parameter changes, approved in a 1/05 process validation report for Heparin Sodium USP, were not demonstrated.

2. There has been no impurity profile established for Heparin Sodium USP and no evaluation for degradants during stability program testing.

3. The manufacturing instructions for Heparin Sodium USP are incomplete in that they do not include a description of manual manipulations of the [ ] during processing steps, they do not include the actual, manually entered [ ] set temperatures and times and, operator observations such as level measurements, used in calculations, during the [ ] step are not recorded.

4. There has been no test method verification performed for the reported USP test methods, Nitrogen Determination, Protein and Total Aerobic Microbial Count, employed in testing of Heparin Sodium USP and Heparin Crude materials, to show that the methods are suitable under actual conditions of use. In addition, there is no routine test for [ ] residue amount at the time of release.

5. Investigations into failed lots and out of trend lots were approved as complete, but did not identify a cause for the problem. For example,

Heparin Sodium USP batch [ ] failed the Nitrogen Determination test and was reprocessed to make [ ] without finding the reason for the slightly high, OOS Nitrogen result.

Investigations into [redacted] of customer [ ] specification @ [ ] for Heparin Sodium USP lots [redacted] and [redacted] were performed without knowing what the failed test measurement actually represented.

Investigations into ROI out of trend results for Heparin Sodium USP lots [ ] identified both results inappropriately as outliers.

6. Heparin Crude lots [ ] received 8/06 from vendor [redacted] that included material from an unacceptable workshop vendor were used in Heparin Sodium USP [ ] marketed to the USA. In addition, prior to 3/06 there are no [ ] records from vendor [ ] showing the source for their crude materials.

7. The inside surface of large, "cleaned" [ ] tanks used in the final [ ] step, after both [ ] were very scratched, with unidentified material adhering to the insides and, the inverted handles held liquid, which spilled to the bottom of the tank when it was uprighted. There was no written procedure showing that the tanks were dedicated to a particular process step. There was no data collected to verify marker and tape volume markings on the outside of the tanks

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	Regina T. Brown Zi-Qiang Gu	Regina T. Brown, Investigator Zi-Qiang Gu, Chemist	Feb. 26, 2008

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and, the cleaning method was not validated. It was noted that equipment cleaning tags were made of paper and taped to the piece of equipment unprotected from liquids used in the processing room environments.

8. Raw material inventory records were incomplete in that samples removed from the containers and the status and amount of materials returned from use by the production processing department were not recorded. For [ ] stored in a freezer, the amount, condition and date of return was not recorded.

9. Control of material flow in the processing area was inadequate in that waste [ ] was carted through a door to the outside in the processing area and not provided for by the material flow written procedure.

10. The outer foil bags containing Heparin Sodium USP lot [ ] manufactured and held since 5/25/07, are not labeled. The drum lid showed the only indications of the lot number.

11. There is no report or data to show that leachables for the [ ] bags used to hold Heparin Sodium USP lot, have been evaluated.

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The observations of objectionable conditions and practices listed on the front of this form are reported:

1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or
2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration.

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC 374(b)) provides:

"Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgment, indicate that any food, drug, device, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under unsanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary."