DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
12420 Parklawn Drive, Room 2032 Rockville, MD 20857	12/9/2019-12/13/2019
	FEI NUMBER 3007045622

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Mr. Joachim Fries, Site Head & Head of Operations

FIRM NAME	STREET ADDRESS
Siegfried Pharma AG	Untere Bruhlstrasse 4
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Zofingen, Aargau, 4800 Switzerland	Drug 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 I OBSERVED:

LABORATORY CONTROL SYSTEM

OBSERVATION 1

Testing and release of drug product for distribution do not include appropriate laboratory determination of satisfactory conformance to the final specifications prior to release.

Specifically, testing and release of (b) (4) (b) (4) Tablets do not include appropriate laboratory determination of satisfactory conformance to the impurities specifications.

(b) (4) Tablets are tested for Impurities by using analytical method (# Z TM 0252-02, Version: 02, Effective Date: 7/15/2019). As per this test procedure HPLC sample run time for impurities analysis is (b) (4) However, when commercial release and stability data is processed for impurities analysis; integration of peaks is inhibited after (b) (4) of run time. There is no assurance that any impurities eluting after (b) (4) would be accounted for towards total impurities. Firm's practice to inhibit integration of peaks at (b) (4) is consistent during commercial release and stability testing of (b) (4) Tablets. Since last inspection the site shipped (b) (4) batches of (b) (4) (b) (4) Tablets into the US market.

OBSERVATION 2

Determinations of conformance to appropriate written specifications for acceptance are deficient for drug products.

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	Saleem A Akhtar, Investigator	X Saleem A Akhtar Investigator Signed By: 2001638440 Date Signed: 12-13-2019 08:13:50	12/13/2019

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Specifically, determinations of conformance to the dissolution specifications are deficient for (b) (4) (b) (4) Tablets. (b) (4) Tablets are tested for Dissolution as per test procedure # Z TM 0158-03, Version: 03, Effective Date: 9/1/2015. During this analysis tablets are (b) (4) (b) (4) The dissolution samples are pulled at (b) (4) time points. Following deficiencies were observed in dissolution analysis for (b) (4) tablets:

A. Dissolution start and end times are not documented.

B. The (b) (4) of the dissolution media and (b) (4) are not verified and documented before, during, and at the end of the dissolution test.

FACILITIES & EQUIPMENT SYSTEM

OBSERVATION 3

Equipment used in the manufacture, processing, packing or holding of drug products is not of appropriate design to facilitate operations for its intended use and cleaning and maintenance.

Specifically, the equipment used to manufacture (b) (4) Tablets is not of appropriate design to facilitate its intended use, cleaning, and maintenance. On 12/9/2019the (b) (4) used (b) (4) step, room # (b) (4) equipment inventory # 30125) to manufacture (b) (4) tablets for the US market was observed to have portion of the inside surface (potential product contact surface) scratched and dented. The impacted surface appeared to be unsmooth. After each use, (b) (4) are dismantled and removed out for cleaning. It was stated when these (b) (4) of the equipment are removed for cleaning; surface scratching is hard to avoid due to the unique shape of the equipment (b) (4) (b) (4) This is a shared equipment and is used to manufacture multiple drug products including (b) (4) (b) (4) Tablets etc.

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OBSERVATION 4

Equipment and utensils are not cleaned at appropriate intervals to prevent contamination that would alter the safety, identity, strength, quality or purity of the drug product.

Specifically, production equipment such as (b) (4) Machine (b) (4) room # (b) (4) equipment inventory # 35152) used to (b) (4) is not appropriately cleaned to prevent contamination that would alter the safety, identity, strength, quality or purity of the drug products. For example;

A. Some stains that appear to be (b) (4) were observed on the tubings (b) (4) Similar (b) (4) stains were also observed on other surfaces of the equipment. This equipment was tagged as clean and the cleaning was performed and verified on 12/5/2019.

B. (b) (4) that appeared to be (b) (4) was observed on the floor of room # (b) (4) where (b) (4) Machine, (b) (4) is housed. This room was tagged as clean and the cleaning was performed and verified on 12/5/2019.

Review of the use logbook for (b) (4) indicated the equipment was last time used to manufacture (b) (4) Tablets (that are (b) (4) on 12/5/2019.

QUALITY SYSTEM

OBSERVATION 5

Written procedures are not followed for evaluations done at least annually and including provisions for a review of investigations conducted for each drug product.

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Specifically, annual product quality reviews for (b) (4) Tablets and (b) (4) Tablets were not done appropriately until the start of the inspection. For example;

A. Annual product quality review report (covering the period of 6/27/2018 to 6/26/2019) for (b) (4) (b) (4) Tablets was approved on 8/26/2019. However, two deviations (# DR-A-050 and DR-A-19-006) and one Change Control (# CR-A-18-124) initiated during the review time were not included in the review.

B. Annual product quality review report (covering the period of 7/15/2018 to 7/14/2019) for (b) (4) (b) (4) Tablets was approved on 8/18/2019. However, one deviation (# DR-A-050) and two Change Control Requests (# CR-A-18-132 and CR-A-19-040) initiated during the review time were not included in the review.

The site signed second versions of these reports on 2nd day of the inspection on 12/10/2019.

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